

# CELL ADAPTATIONS

# CELL INJURY

# CELL DEATH

DR. PRIYANKA SACHDEV , MD

*Scan or Click to watch  
Cell Adaptation & Injury*



*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



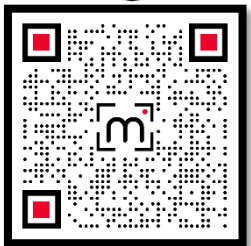
*Scan or Click to watch  
Haemodynamic Disorder*



# TYPES OF CELLS

1. Labile cells
2. Stable cells
3. Permanent cells

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# Labile

## Continuous regeneration from stem cells (self-renewal)

- a) Hematopoietic cells in bone marrow
- b) Surface epithelia – skin, oral cavity, vagina, cervix
- c) Duct epithelia – salivary glands, pancreas, biliary tract
- d) Mucosae – GIT, uterus, fallopian tubes, urinary bladder

# Stable

## Regeneration as response to injury

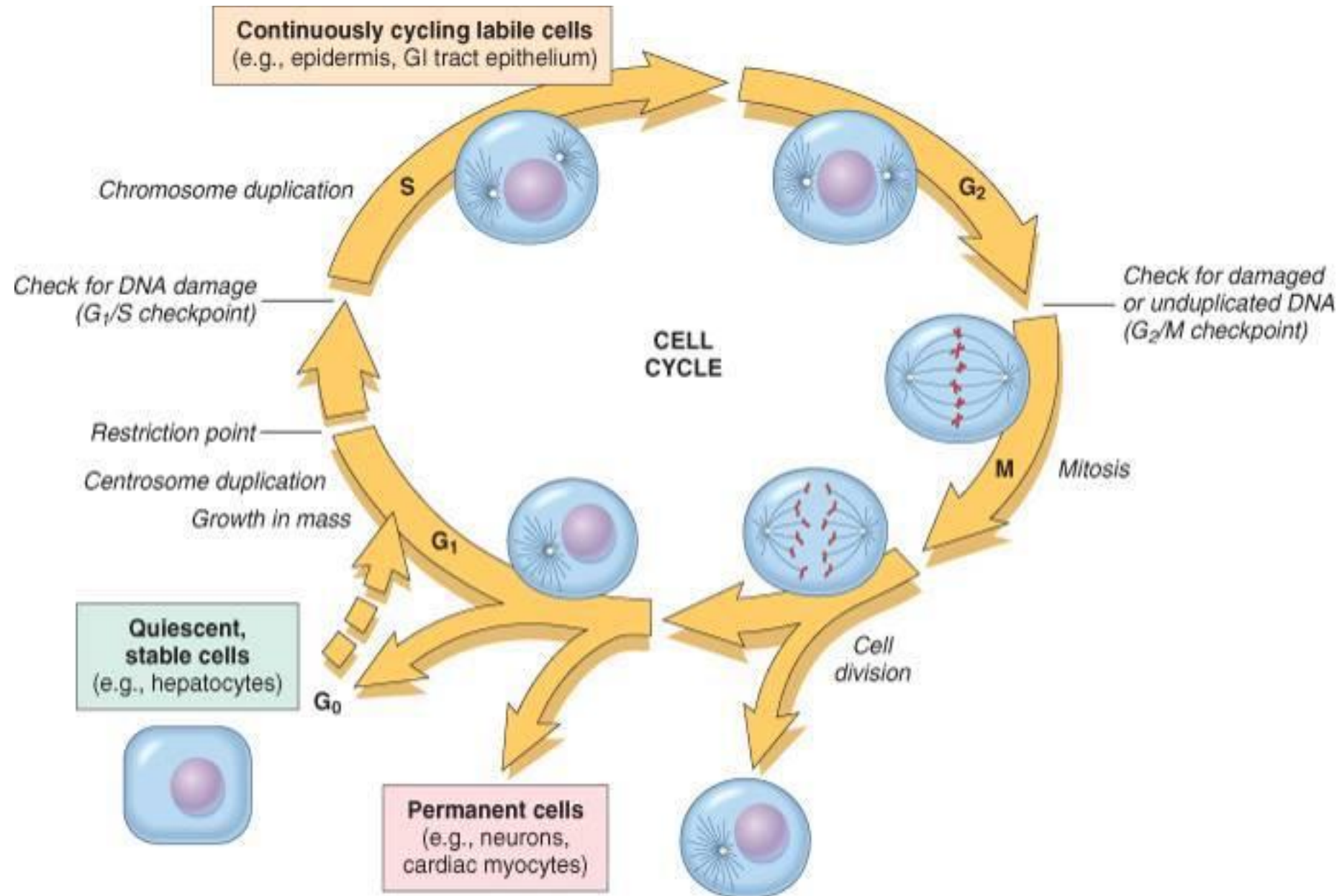
- a) Parenchyma – liver, pancreas, renal tubules
- b) Mesenchymal cells, endothelium



# Permanent

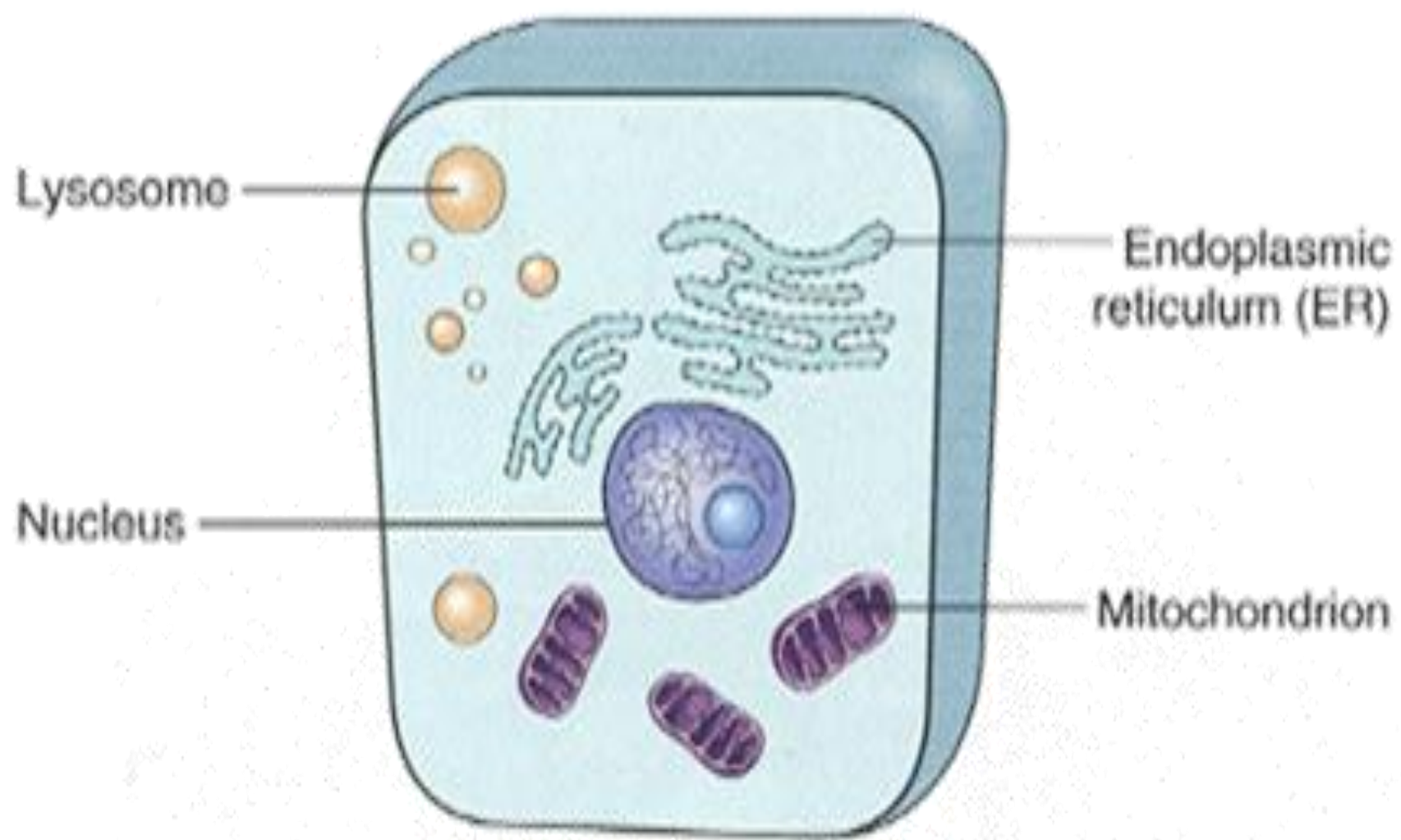
**Nonproliferative in postnatal life**

- a) Neurons
- b) Cardiomyocytes



# INTRODUCTION

- **Cells** are the **structural and functional units** of tissues and organs.
- Normal cells have a fairly narrow range of function or steady state: **Homeostasis**



A. Normal cell

**Normally cells in homeostasis**



**Physiological and pathological stress**



**Cellular adaptation** (reversible on withdrawal of stimulus)



**If the irritant stimulus persists for long time**



**Cell injury**



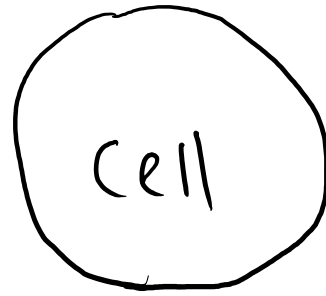
**Reversible cell injury**

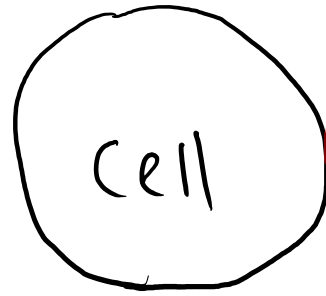


**Irreversible cell injury (Cell death)**

**-Apoptosis**

**-Necrosis**





STRESS  
(physiological or  
pathological)

**Normally cells in homeostasis**



**Physiological and pathological stress**



**Cellular adaptation** (reversible on withdrawal of stimulus)



**If the irritant stimulus persists for long time**



**Cell injury**



**Reversible cell injury**

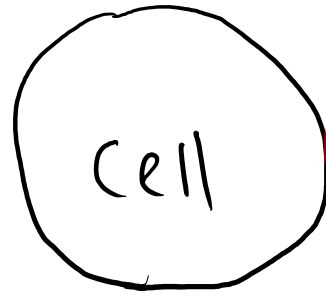


**Irreversible cell injury (Cell death)**

**-Apoptosis**

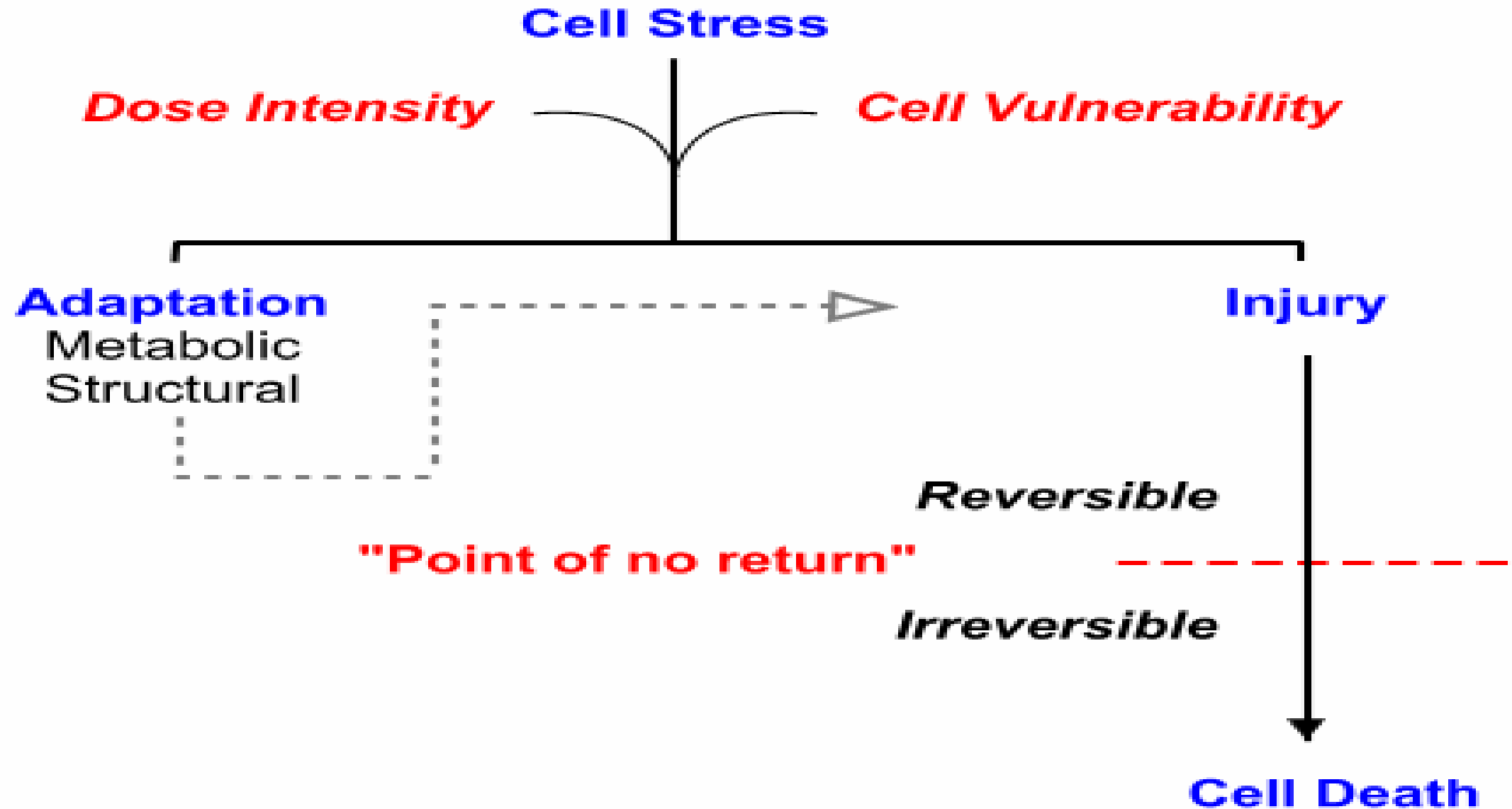
**-Necrosis**

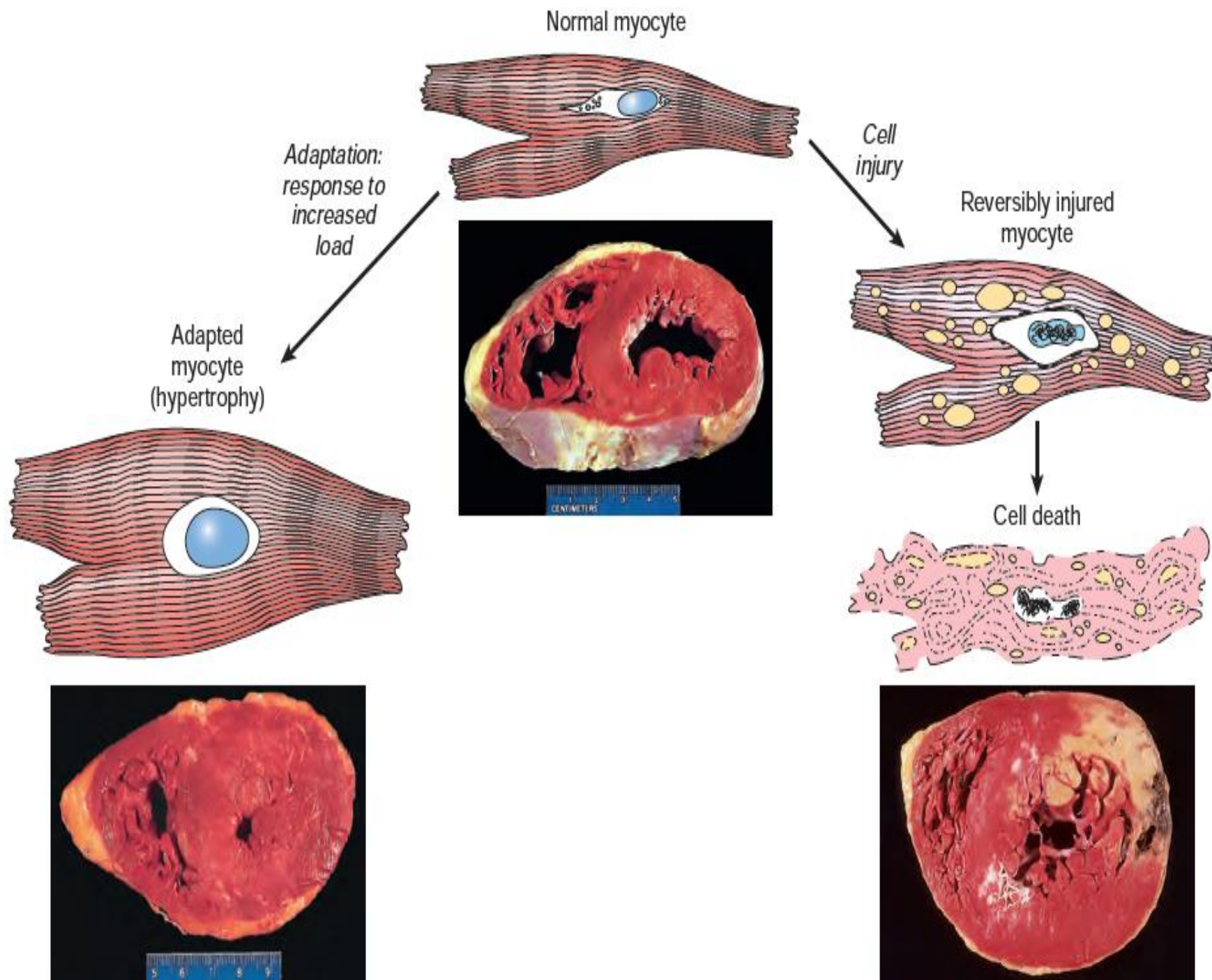




STRESS  
(physiological or  
pathological)

- **Cell injury** results when cells are stressed so severely that they are **no longer able to adapt**
- i.e., when the limits of adaptive response to a stimulus are exceeded, cell injury occurs.

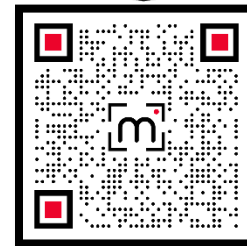




- **Cell injury is reversible up to a certain point, but if the stimulus persists or is severe enough from the beginning, the cell reaches a “point of no return” and suffers irreversible injury and ultimate cell death.**

- **Adaptation, reversible injury and irreversible injury & cell death** are stages of progressive impairment of the cell's normal function and structure.

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# **CELL ADAPTATIONS**

## **CELL INJURY**

## **CELL DEATH**

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# CELL ADAPTATIONS





# DEFINITION

- **Adaptations** are **reversible**, functional and structural responses to physiologic stress (e.g., pregnancy) and pathologic stress, during which new but altered steady states are achieved, allowing the cell to survive and continue to function

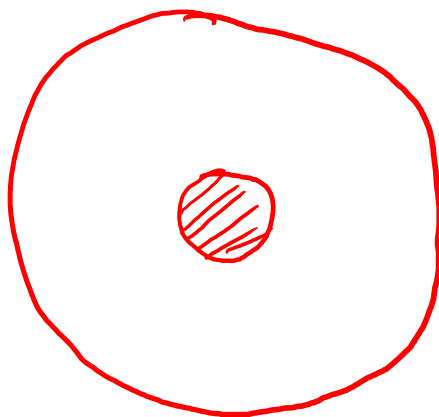
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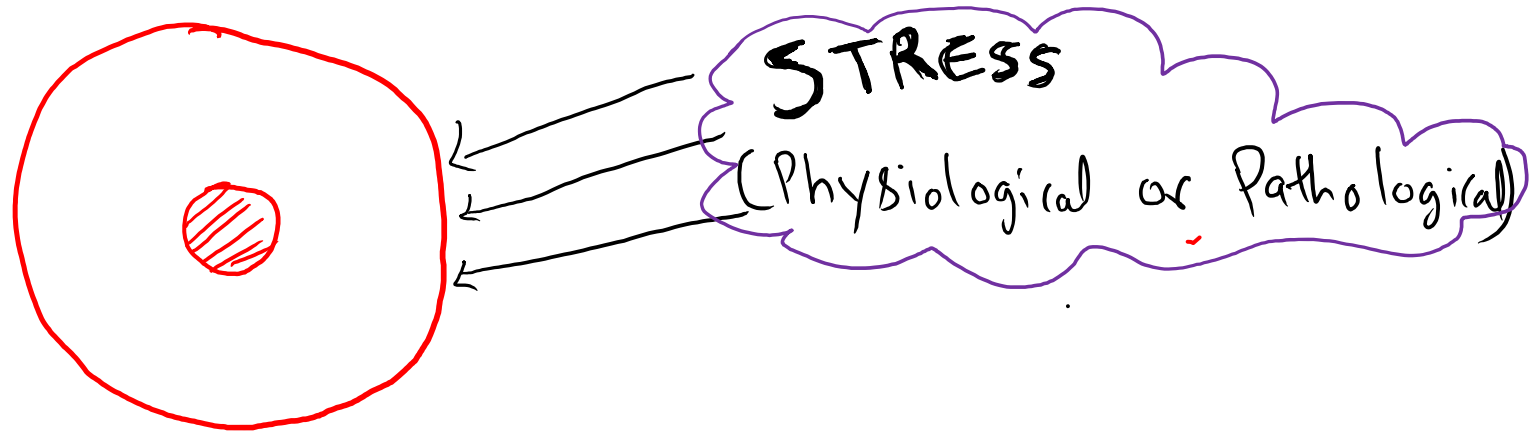


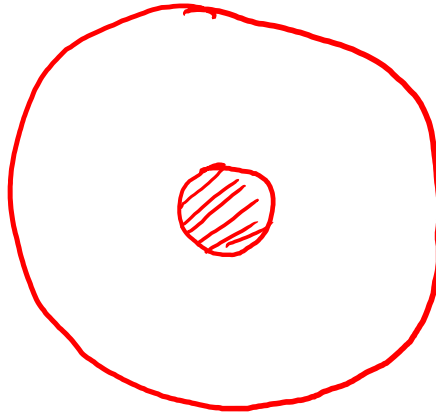
# DEFINITION

## Adaptations →

- ❑ Are **reversible**
- ❑ **Structural responses** to physiologic stress (e.g., pregnancy) and pathologic stress
- ❑ During which new but altered **steady states** are achieved
- ❑ Allowing the cell to **survive and continue to function**







**In order to survive and continue to function**



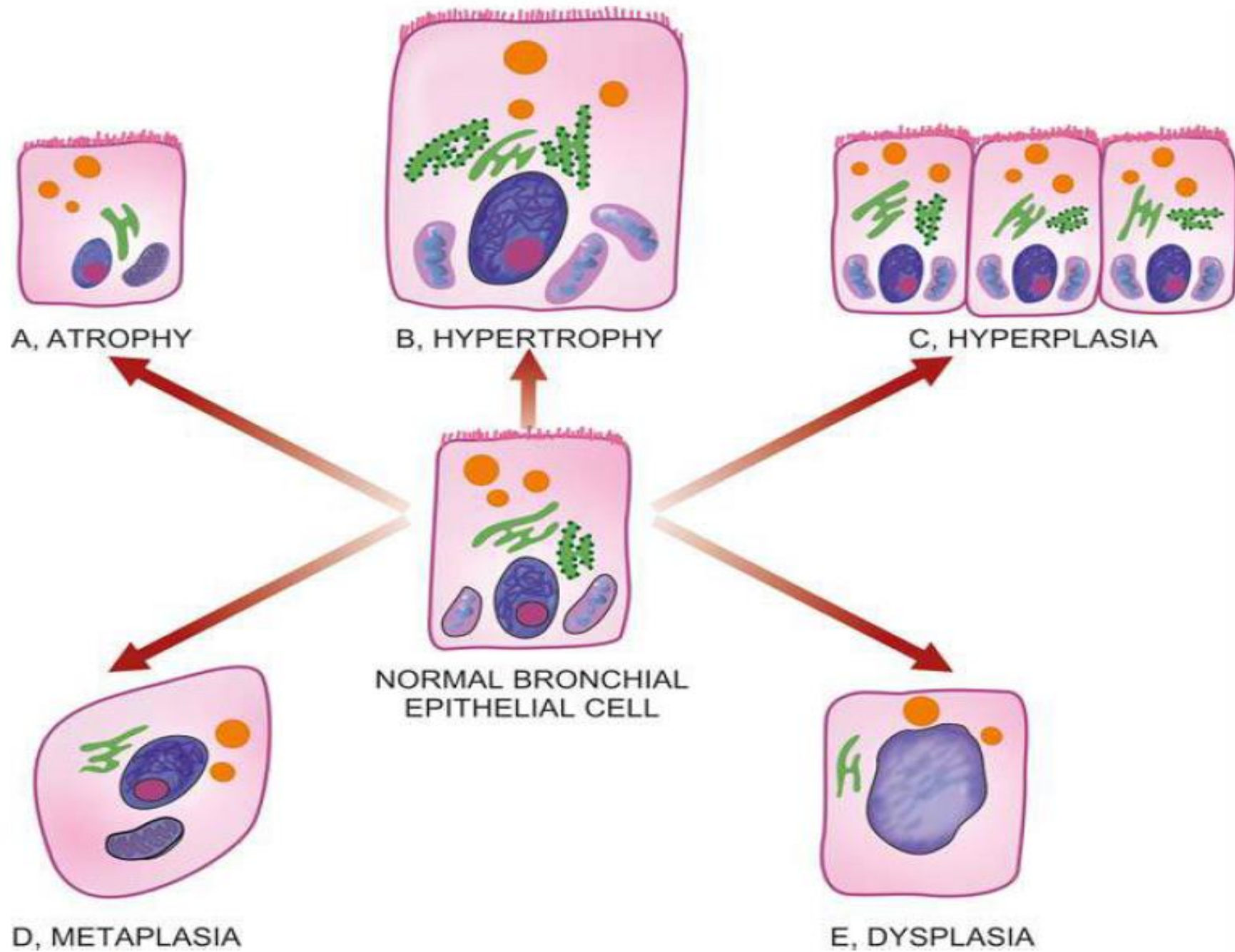
**Cells adjust their structure and functions**

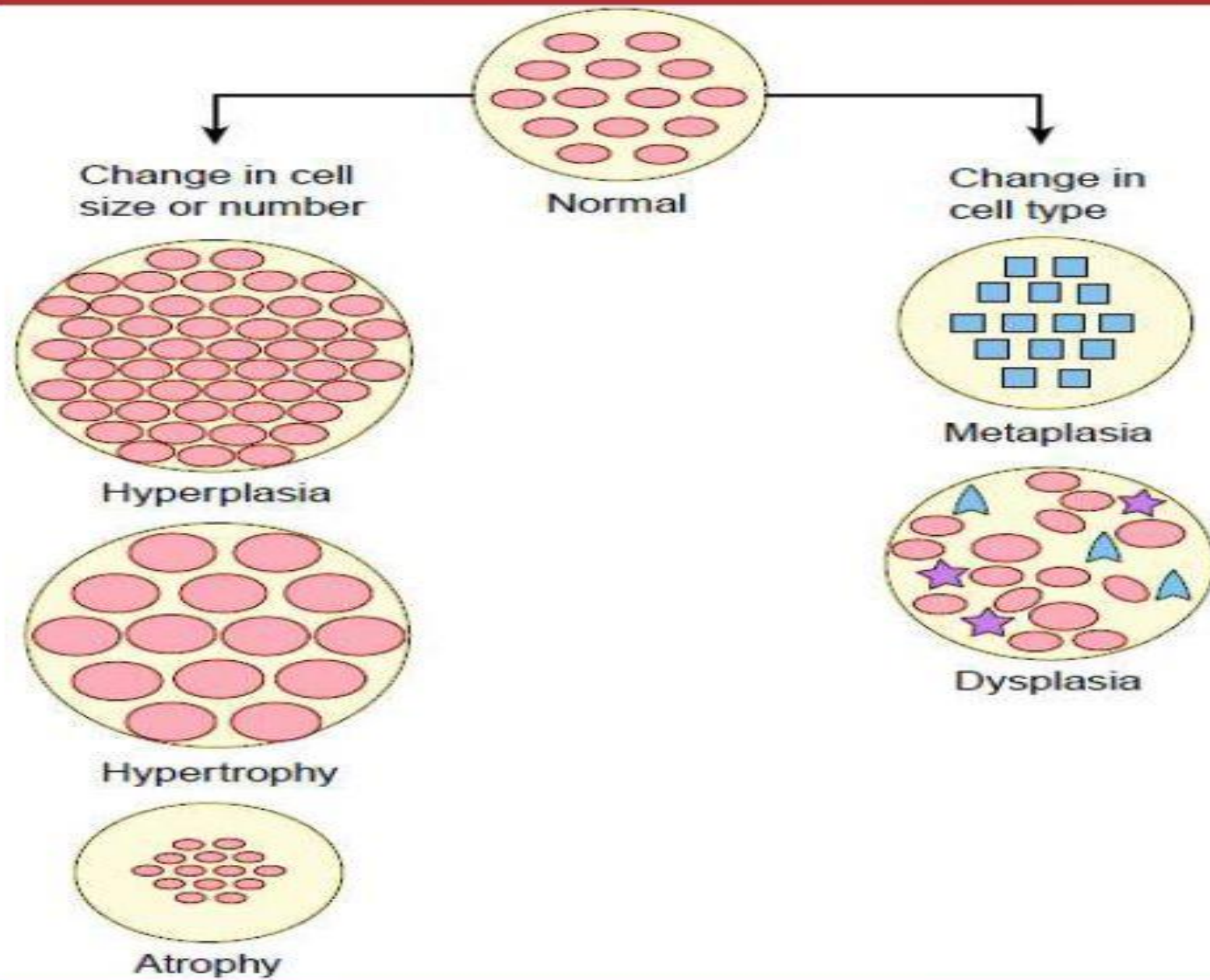


**Cellular adaptation**  
(reversible on withdrawal of stimulus)

# 5 TYPES OF ADAPTATIONS

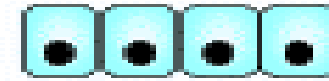
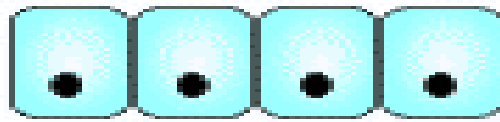
1. **Hypertrophy** → Increase in the size of cells
2. **Hyperplasia** → Increased number of cells
3. **Atrophy** → Decrease in the size of cells / shrinkage of cells
4. **Metaplasia** → Transformation or replacement of one adult cell type with another
5. **Dysplasia** → means 'disordered cellular development'



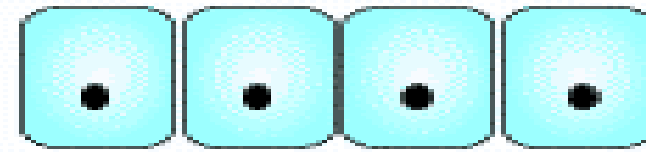
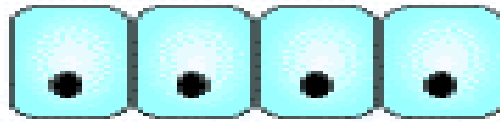




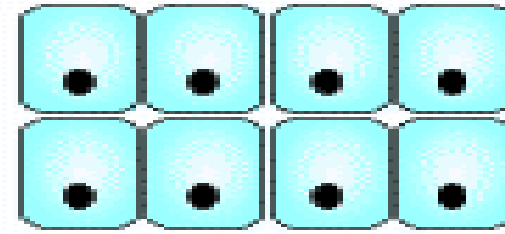
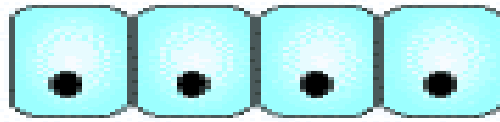
## Cellular Adaptation to Stress



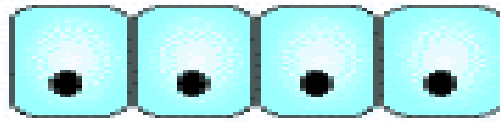
**Atrophy**



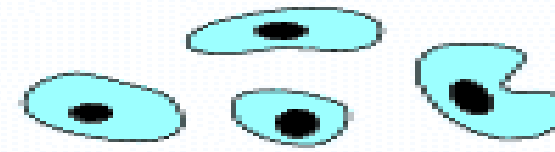
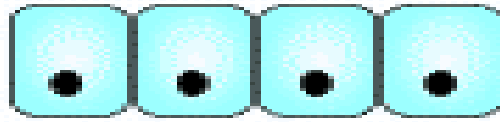
**Hypertrophy**



**Hyperplasia**



**Metaplasia**

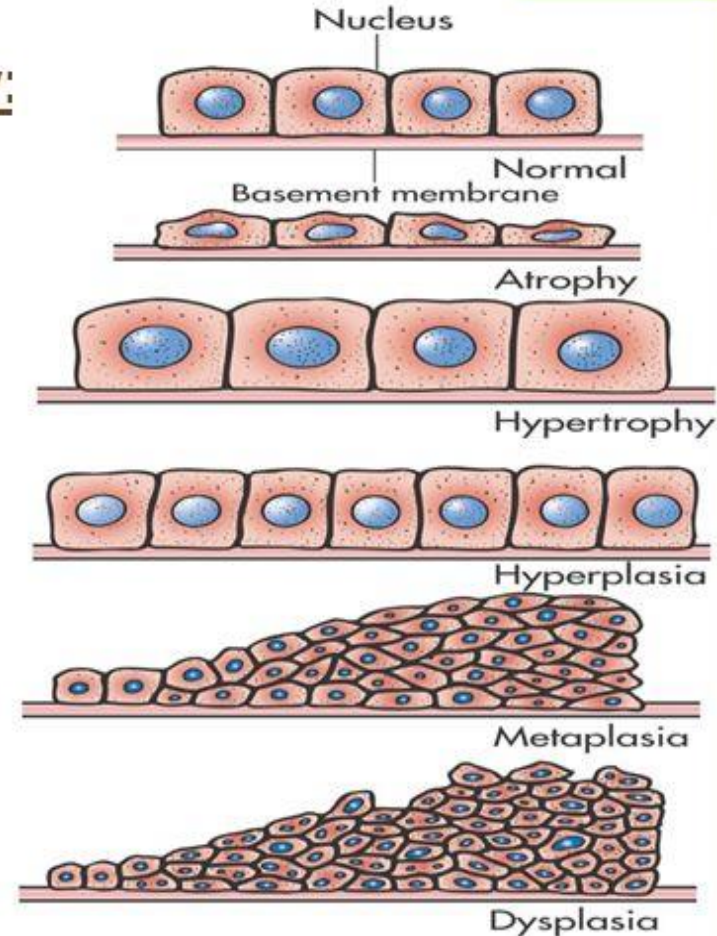


**Dysplasia**

# Cell Adaptation to Injury

## Five Cellular Adaptations to Injury:

1. Atrophy
2. Hypertrophy
3. Hyperplasia
4. Metaplasia
5. Dysplasia



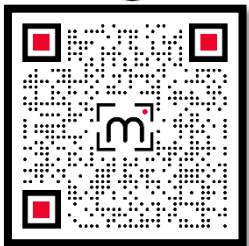
From Lewis SM, Collier IC, Heitkemper MM: *Medical-surgical nursing: assessment and management of clinical problems*, ed 5, St Louis, 2000, Mosby. Mosby items and derived items copyright © 2004, 2000 by Mosby, Inc.

# Headings

- **Defination**
- **Diagram**
- **Mechanism**
- **Types with examples**
- **Morphology**

# **HYPERPLASIA**

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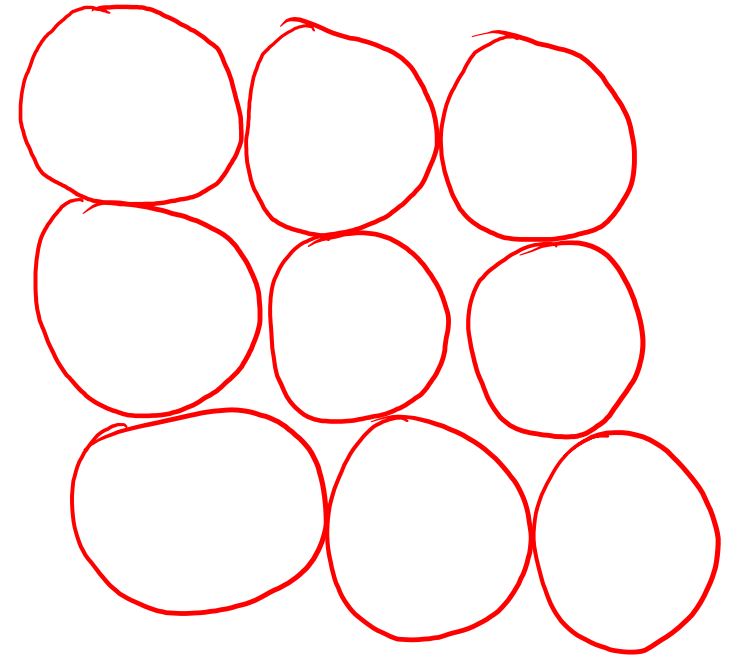


# Headings

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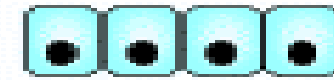
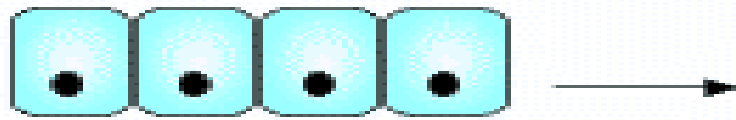
# DEFINITION

- Increase in the **number of cells** , **not size of cell**, resulting in enlargement of the organ or tissue.
- seen in tissues made up of **labile cells and stable cells (not in permanent cells)** – they can divide.
- May or may not be seen together with hypertrophy

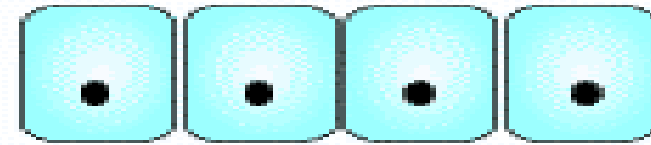
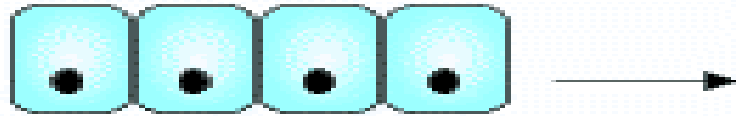


Hyperplasia

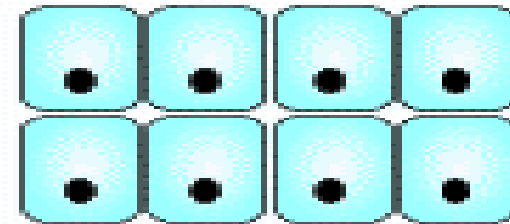
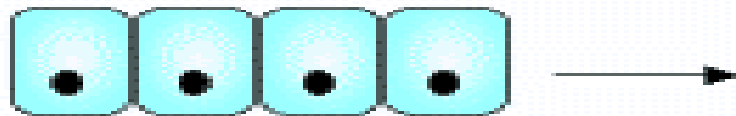
## Cellular Adaptation to Stress



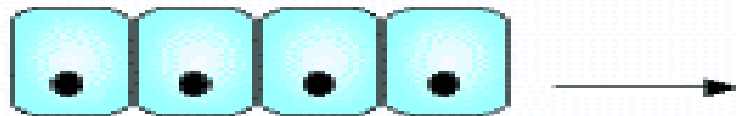
**Atrophy**



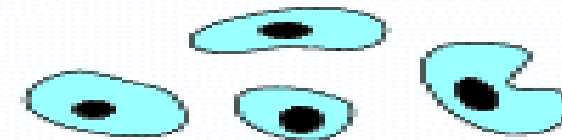
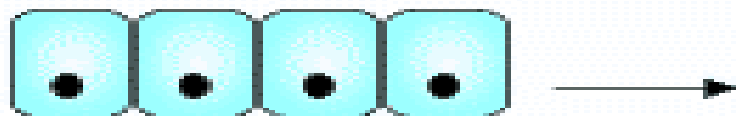
**Hypertrophy**



**Hyperplasia**



**Metaplasia**

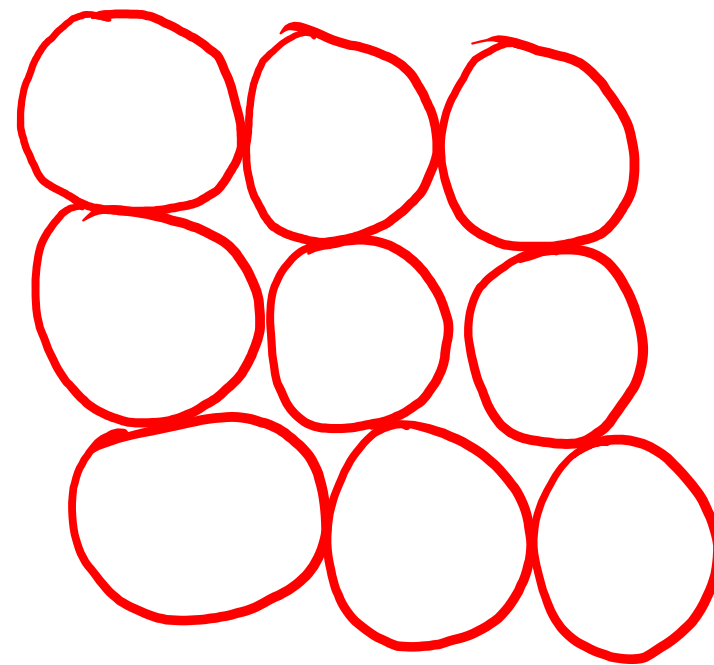
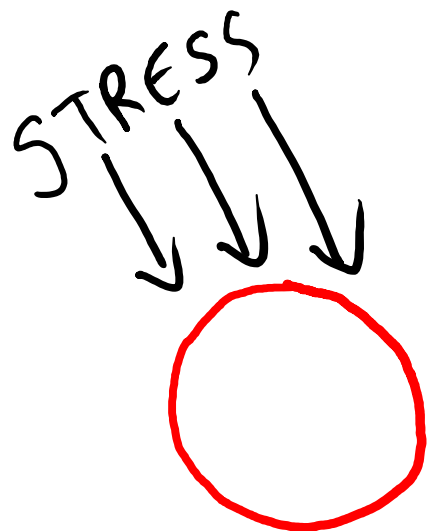


**Dysplasia**



# MECHANISM

- Increased production of growth factors, growth factor receptors
- Eg. after partial hepatectomy growth factors are produced in the liver that engage receptors on the surviving cells and activate signaling pathways that stimulate cell proliferation → Hypertrophy



Hyperplasia

# Headings

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# **HYPERPLASIA**



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graph TD; A[HYPERPLASIA] --> B[Physiological]; A --> C[Pathological]
```

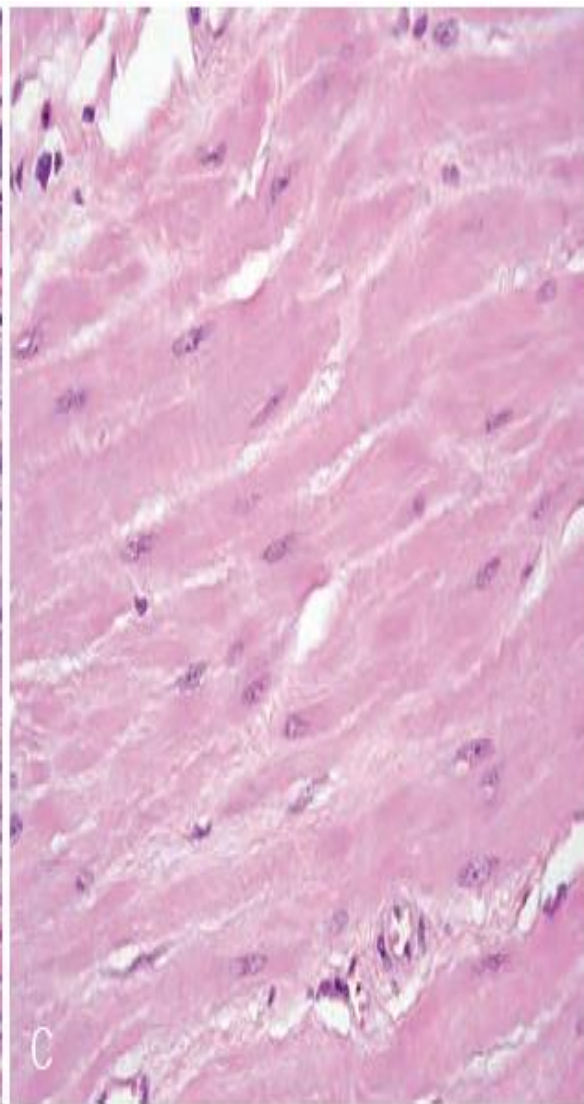
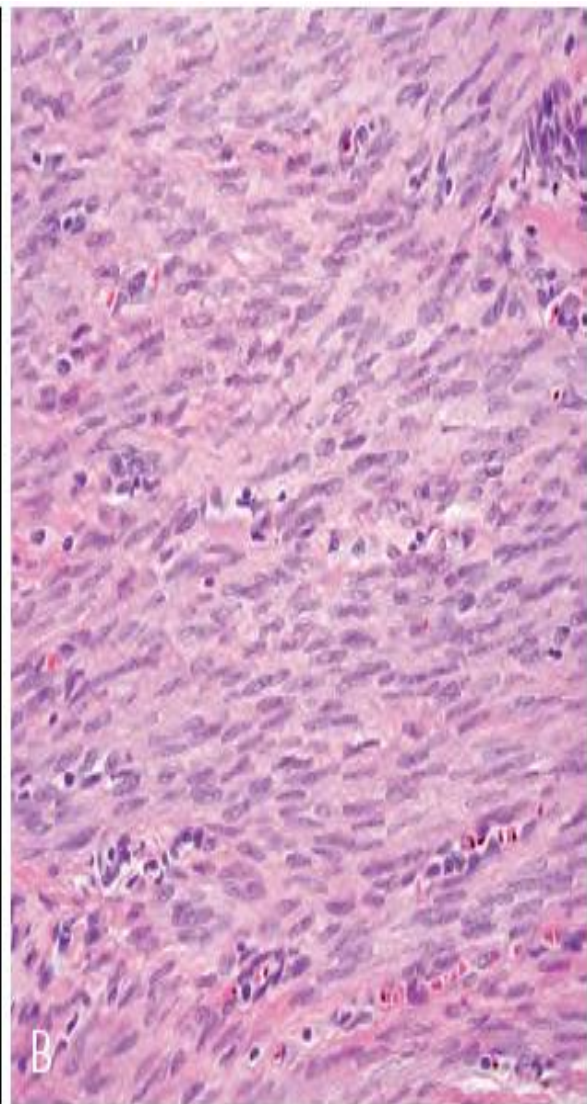
**Physiological**

**Pathological**

# Physiologic hyperplasia

## Hormonal hyperplasia

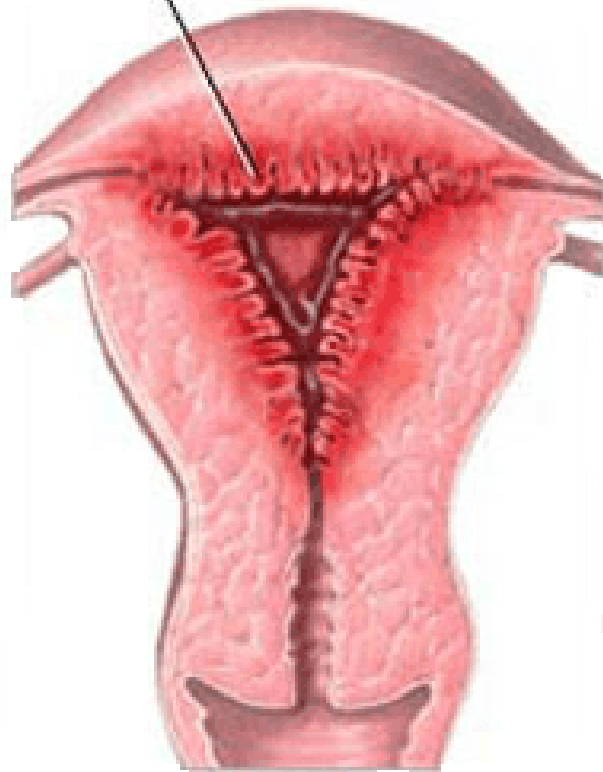
1. Hyperplasia of **female breast** at puberty, pregnancy and lactation.
2. Enlarged size of the **uterus in pregnancy** is an example of physiologic hypertrophy as well as hyperplasia.
3. Proliferation of **endometrium** after a normal menstrual cycle.



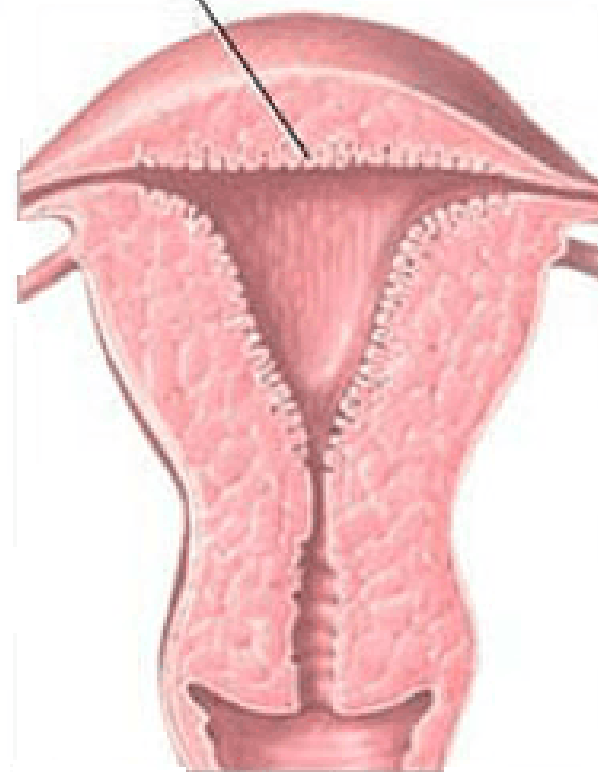
# Pathologic hyperplasia

1. **Endometrial hyperplasia** following oestrogen excess.
2. Formation of **skin warts** from hyperplasia of epidermis due to human papilloma virus (HPV)
3. **Compensatory hyperplasia** →
  - Regeneration of the liver following partial hepatectomy.
  - Regeneration of epidermis after skin abrasion.
  - Following nephrectomy on one side, there is hyperplasia of nephrons of the other kidney.

Endometrial hyperplasia



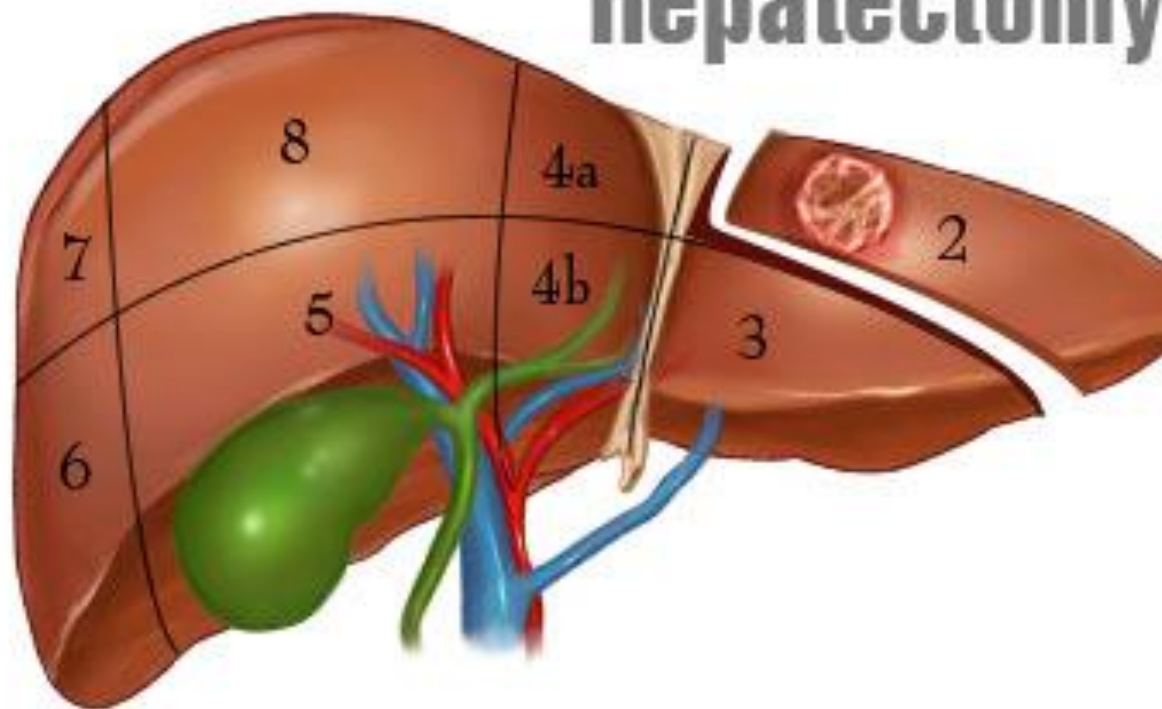
Normal endometrium







# Hepatectomy



# Headings

- **Defination**
- **Diagram**
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- **Morphology**

# MORPHOLOGIC FEATURES

1. **Enlargement** of the affected organ
2. **Increase in the number of cells.**
3. **Increased mitoses** of the cells

# 5 TYPES OF ADAPTATIONS

1. **Hypertrophy** → Increase in the size of cells
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**HYPERTROPHY**

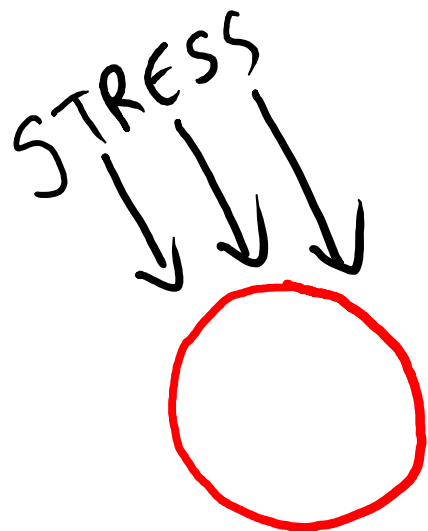
# Headings

- **Defination**
- **Diagram**
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# DEFINITION

- Increase in the **size of cells**, **not number of cells**, leading to an increase in the size of the organ
- Seen in tissues made up of **terminally differentiated cells (stable cells)** – they can no longer divide,  $\therefore$  their only response to the stress is to increase in size not number.

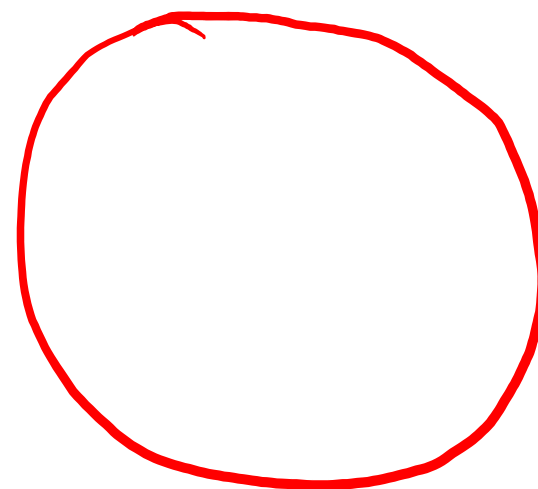




Adaptation

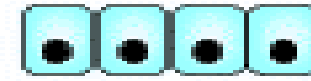
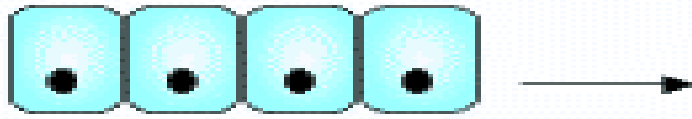


A red arrow pointing from the small circle to the large circle, with the word 'Adaptation' written above it.

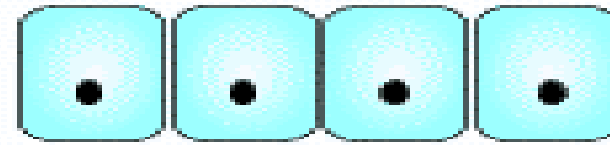
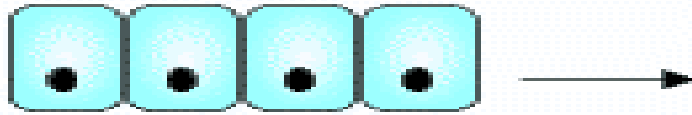


Hypertrophy

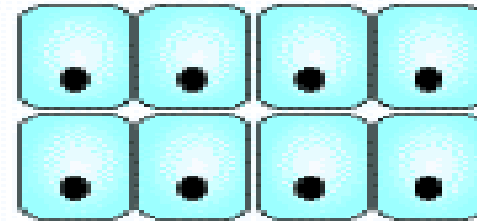
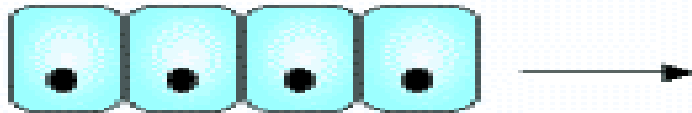
## Cellular Adaptation to Stress



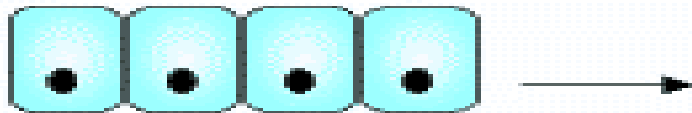
**Atrophy**



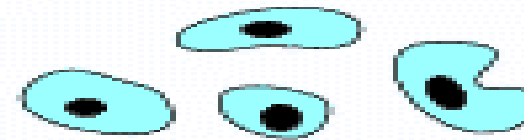
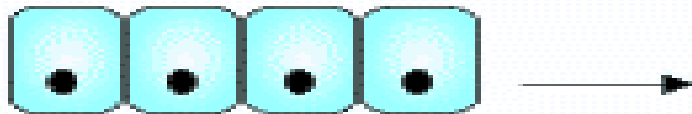
**Hypertrophy**



**Hyperplasia**



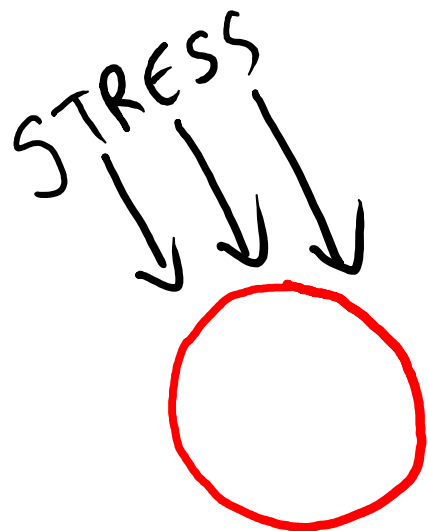
**Metaplasia**



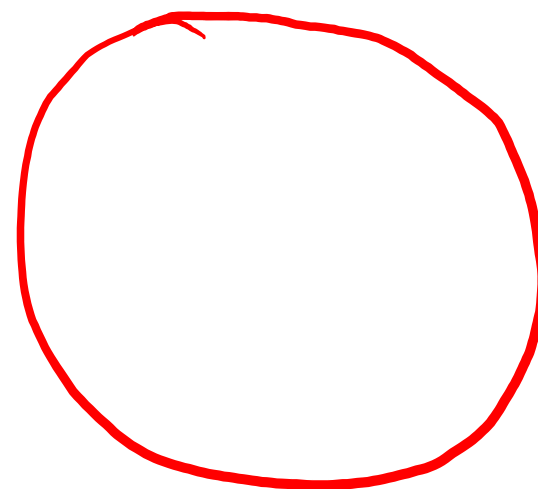
**Dysplasia**

# Mechanism

- Increased size is not due to cellular swelling, its due to **more structural components / cellular proteins**



Adaptation →



Hypertrophy

# Headings

- **Defination**
- **Diagram**
- **Mechanism**
- **Types with examples**
- **Morphology**

# **HYPERTROPHY**



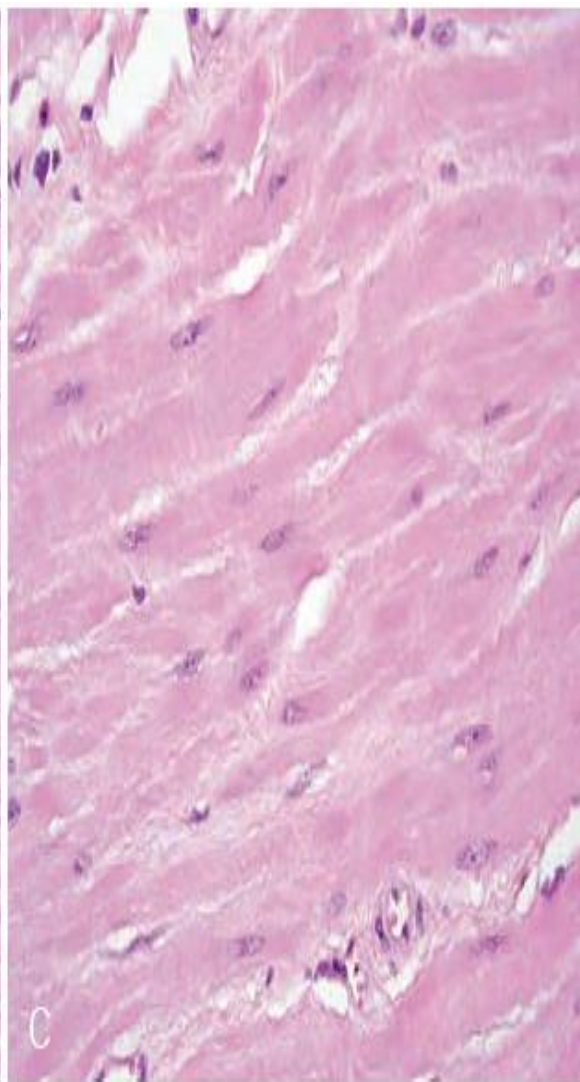
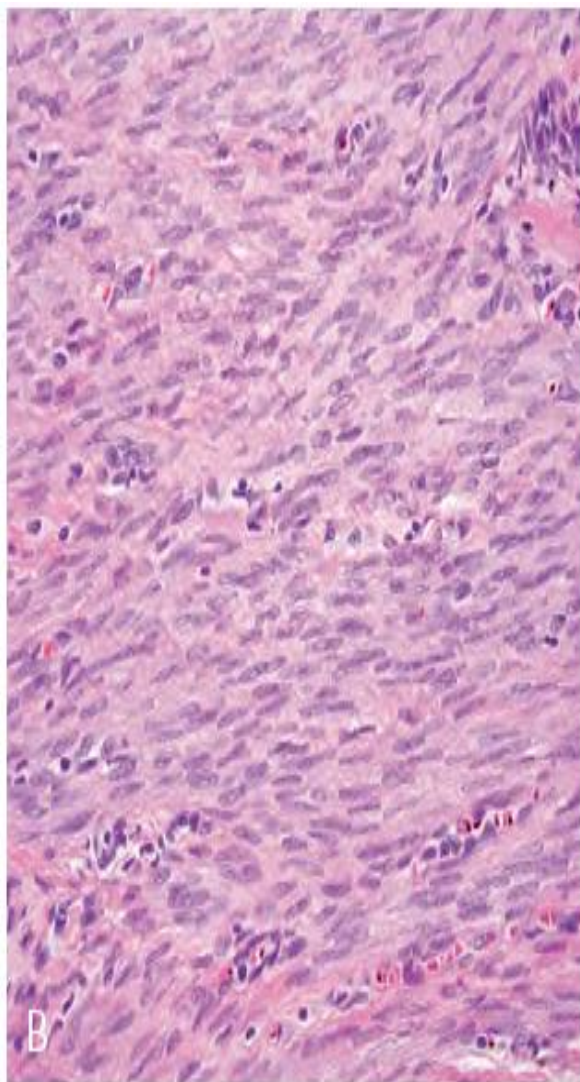
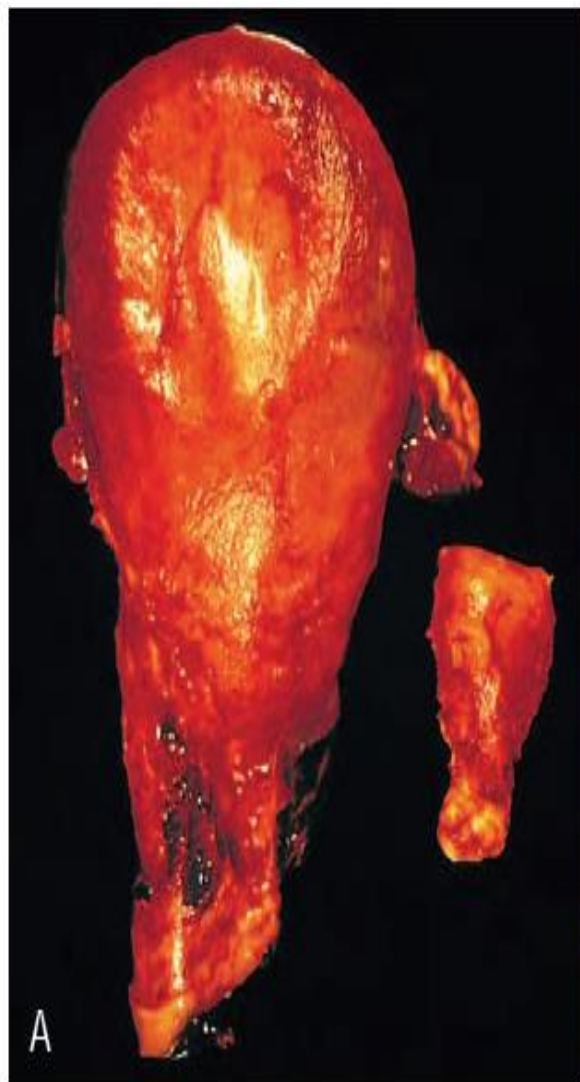
```
graph TD; A[HYPERTROPHY] --> B[Physiological]; A --> C[Pathological]
```

**Physiological**

**Pathological**

# Physiologic hypertrophy

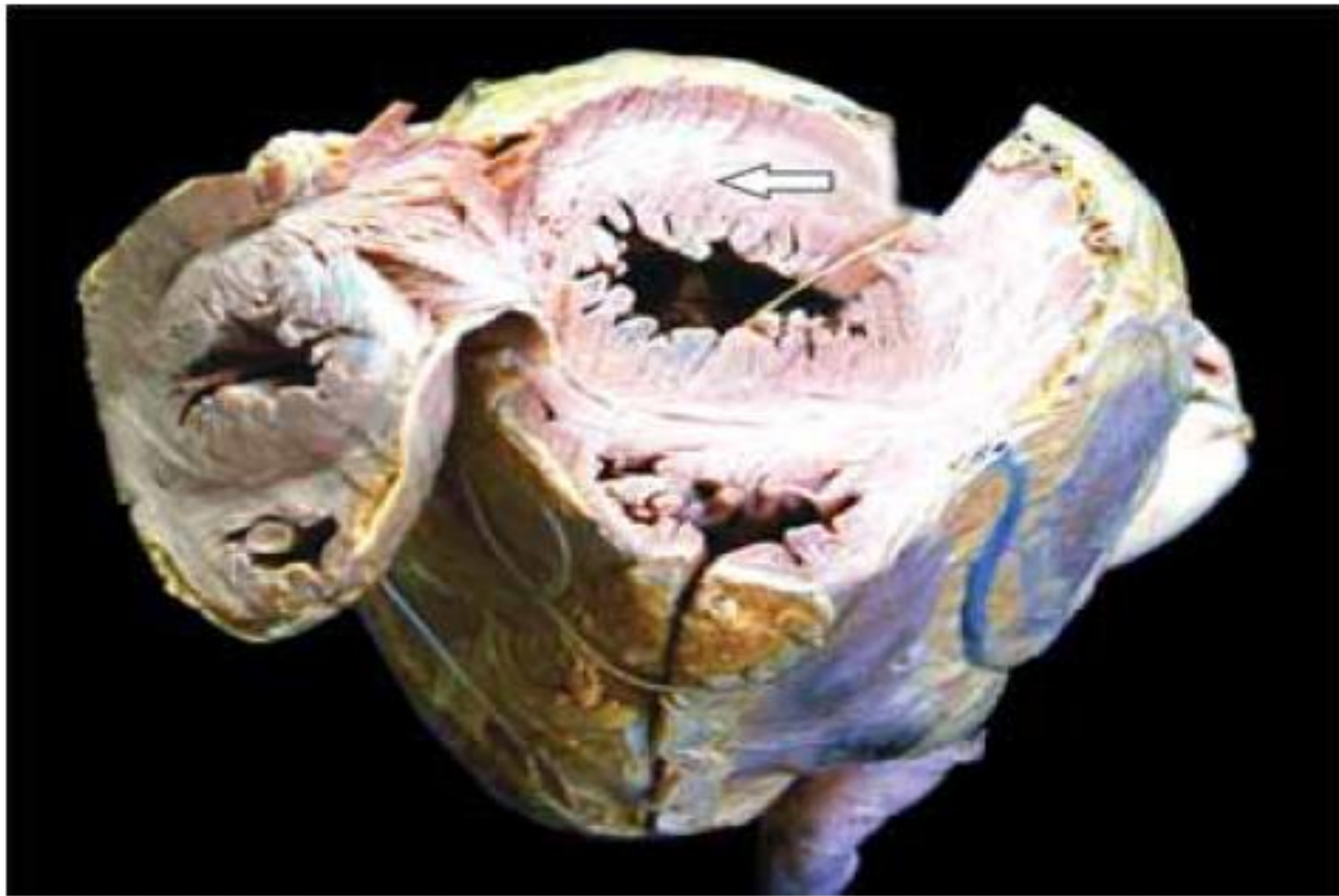
1. Enlarged size of the **uterus in pregnancy** is an example of physiologic hypertrophy as well as hyperplasia.



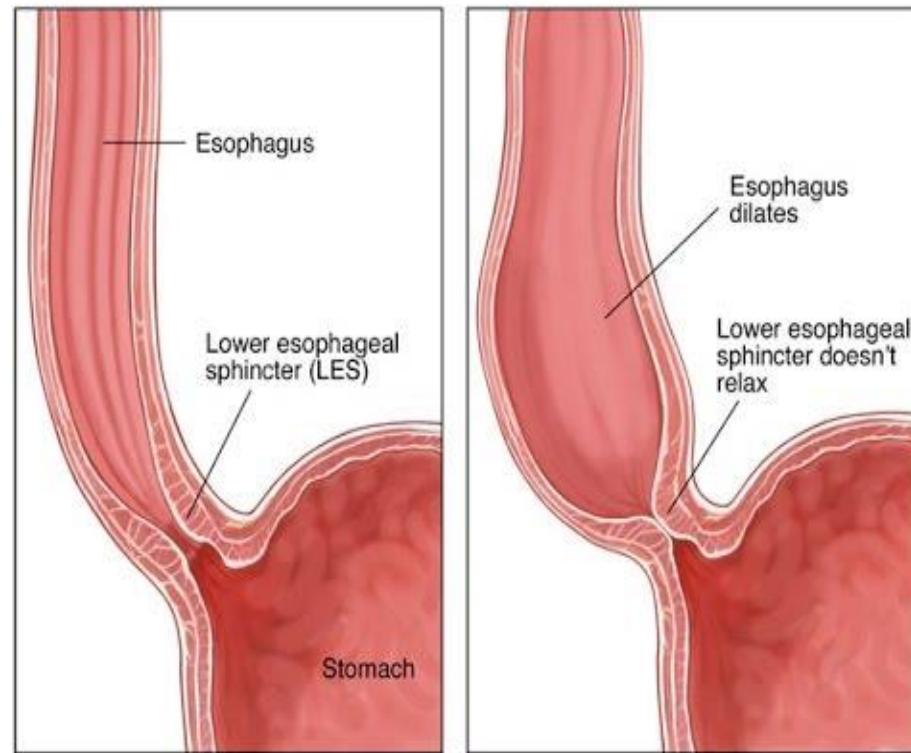


# Pathologic hypertrophy

1. **Hypertrophy of cardiac muscle** occurs in Systemic hypertension, Aortic valve diseases, Mitral insufficiency
2. **Hypertrophy of smooth muscle** e.g. Cardiac achalasia (in oesophagus), Pyloric stenosis (in stomach), Muscular arteries in hypertension.
3. **Hypertrophy of skeletal muscle** e.g. hypertrophied muscles in athletes and manual labourers.



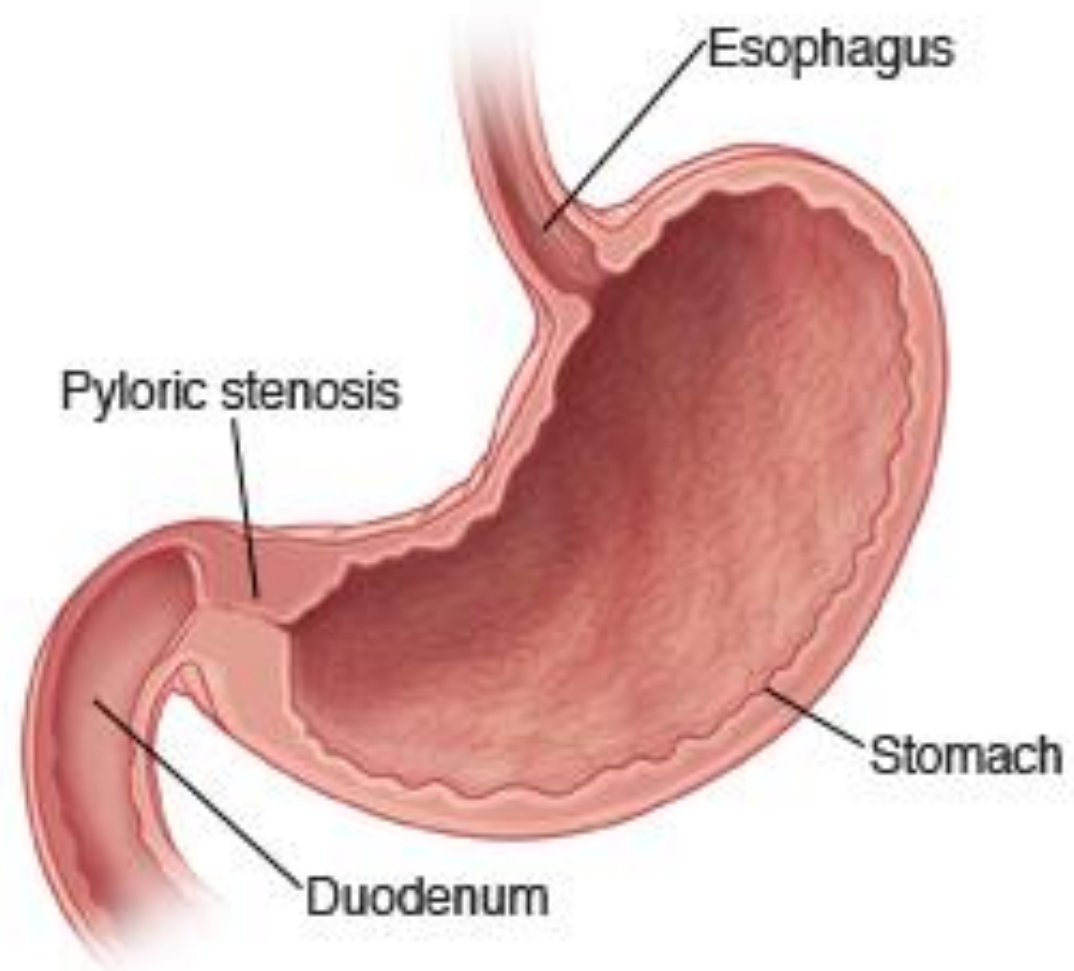
**Figure 2.37** Cardiac hypertrophy. Weight of the heart is increased. The chambers opened up at the apex show concentric thickening of left ventricular wall (white arrow) with obliterated lumen (hypertrophy without dilatation).



Normal

Achalasia

### Esophageal Achalasia





- **Compensatory hyperplasia →**

- Regeneration of the liver following partial hepatectomy.
- Regeneration of epidermis after skin abrasion.
- Following nephrectomy on one side, there is hyperplasia of nephrons of the other kidney.

# Headings

- **Defination**
- **Diagram**
- **Mechanism**
- **Types with examples**
- **Morphology**

# MORPHOLOGIC FEATURES

1. The organ is **enlarged**
2. Increase in size of cell due to **increased synthesis of DNA and RNA, increased protein synthesis and increased number of organelles such as mitochondria, ER and myofibrils**



# 5 TYPES OF ADAPTATIONS

1. **Hypertrophy** → Increase in the size of cells
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# ATROPHY

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# Headings

- **Defination**
- **Diagram**
- **Mechanism**
- **Types with examples**
- **Morphology**

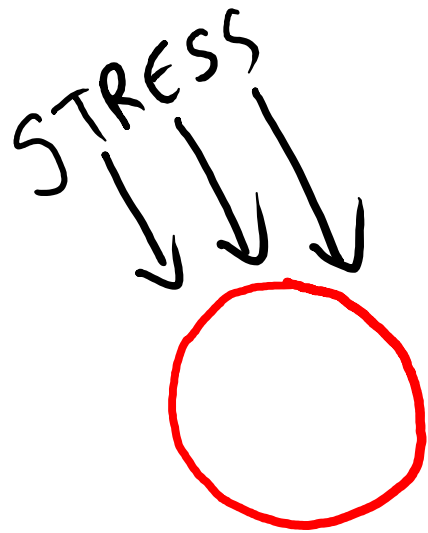


# DEFINITION

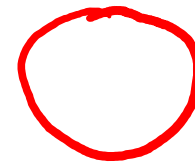
- **Decrease in cell size and number of cells** (with or without accompanying shrinkage of the organ or tissue)
- Atrophied cells are smaller than normal but they are **still viable** – they do not necessarily undergo apoptosis or necrosis

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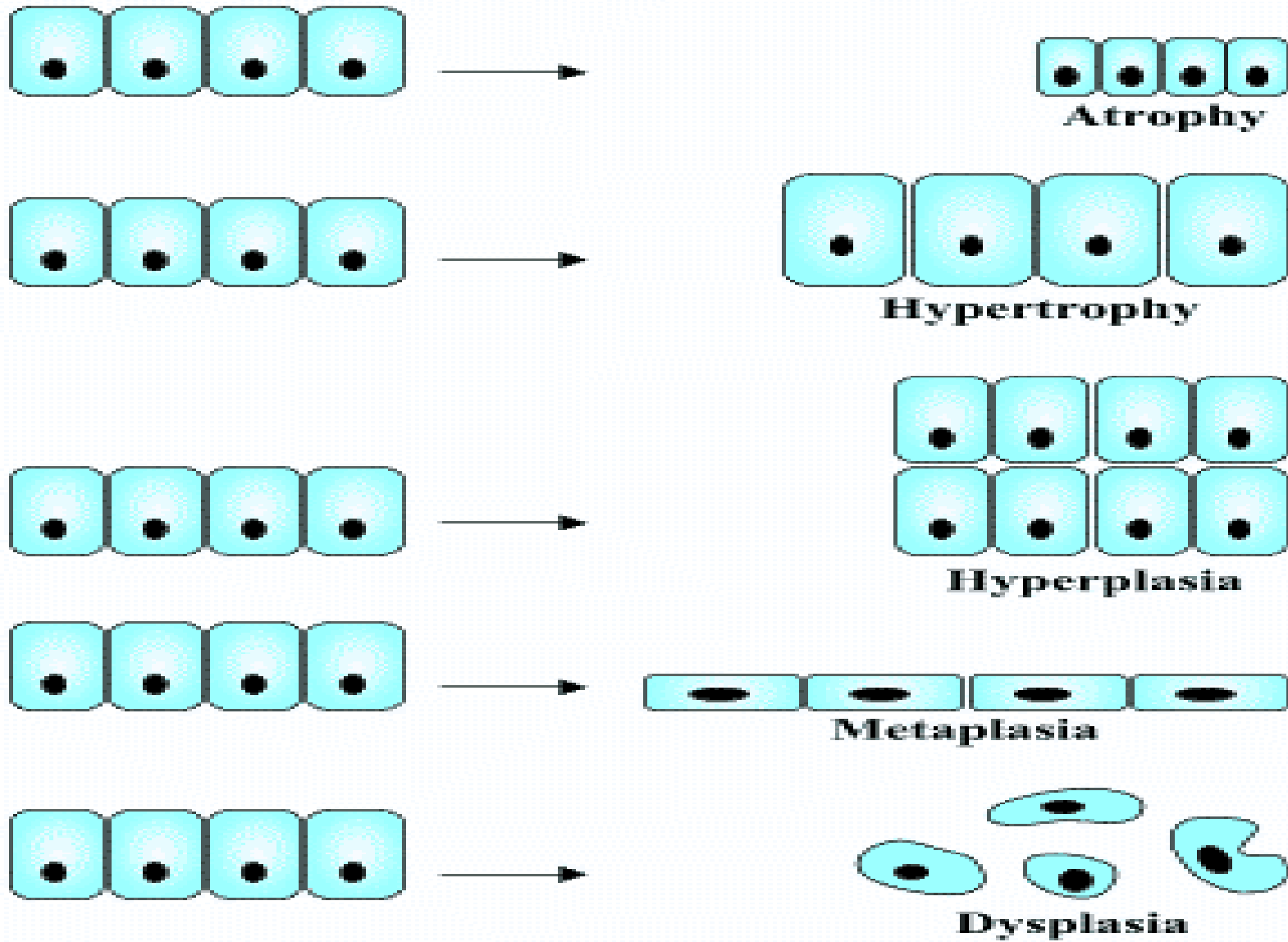


Adaptation



Atrophy

## Cellular Adaptation to Stress



# Mechanism

- Shrinkage in cell size is due to **reduction in cell organelles, chiefly mitochondria, myofilaments and ER**

# Headings

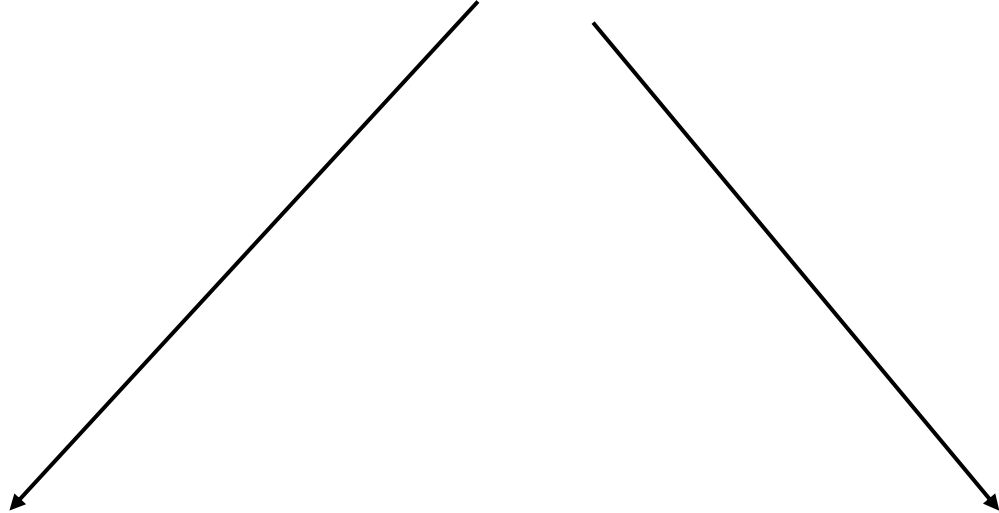
- **Defination**
- **Diagram**
- **Mechanism**
- **Types with examples**
- **Morphology**



**ATROPHY**

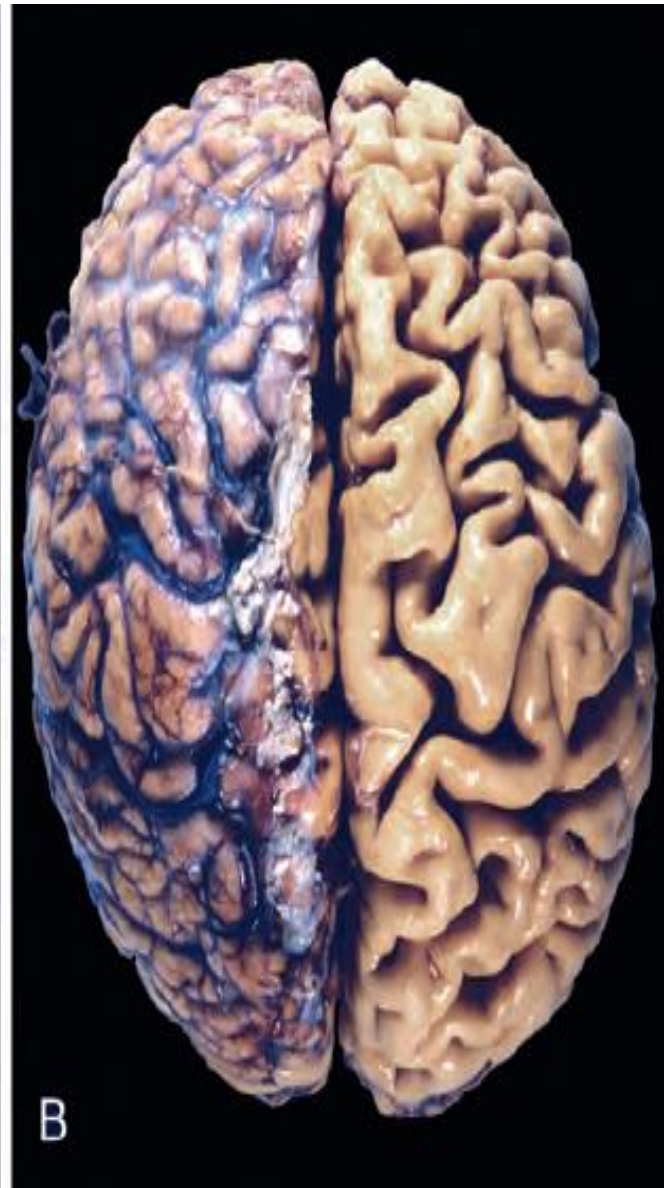
**Physiological**

**Pathological**



# Physiologic atrophy

1. Atrophy of **lymphoid tissue** with age.
2. Atrophy of **thymus** in adult life.
3. Atrophy of **gonads** after menopause.
4. Decrease in the size of the **uterus** that occurs shortly after parturition
5. Atrophy of **brain** with ageing.
6. Osteoporosis with reduction in size of **bony trabeculae** due to ageing.



# Pathologic atrophy

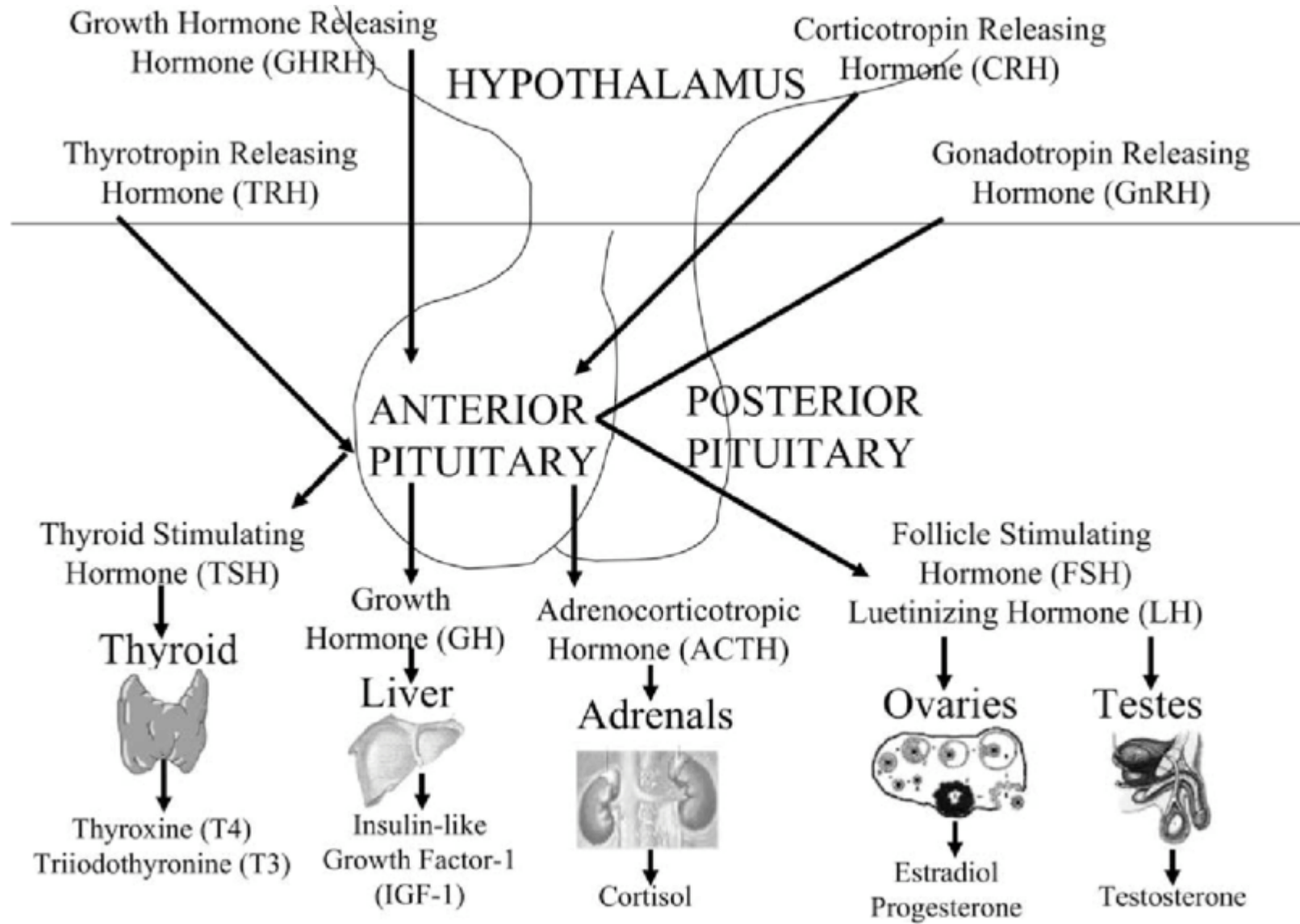
1. **Starvation atrophy** → general weakness, emaciation and anaemia known as cachexia seen in cancer and severely ill patients.
2. **Ischaemic atrophy** → atrophic kidney in atherosclerosis of renal artery, Atrophy of the brain in cerebral atherosclerosis.
3. **Neuropathic atrophy** → e.g. Poliomyelitis, Motor neuron disease
4. **Disuse atrophy** → e.g. Wasting of muscles of limb immobilised in cast, Atrophy of the pancreas in obstruction of pancreatic duct.



**5. Endocrine atrophy** → eg. Hypopituitarism may lead to atrophy of thyroid, adrenal and gonads

**6. Pressure atrophy** → eg. Erosion of the skull by meningioma , Erosion of the sternum by aneurysm of arch of aorta.

**7. Idiopathic atrophy** → where no obvious cause is present



# MORPHOLOGIC FEATURES

1. The organ is **small**
2. **The cells become smaller in size but are not dead cells.**
3. Shrinkage in cell size is due to **reduction in cell organelles, chiefly mitochondria, myofilaments and ER**
4. Increase in the number of **autophagic vacuoles**



# 5 TYPES OF ADAPTATIONS

1. **Hypertrophy** → Increase in the size of cells
2. **Hyperplasia** → Increased number of cells
3. **Atrophy** → Decrease in the size of cells / shrinkage of cells
4. **Metaplasia** → Transformation or replacement of one adult cell type with another
5. **Dysplasia** → means 'disordered cellular development'

# METAPLASIA

follow us



# Headings

- **Defination**
- **Diagram**
- **Mechanism**
- **Types with examples**
- **Morphology**

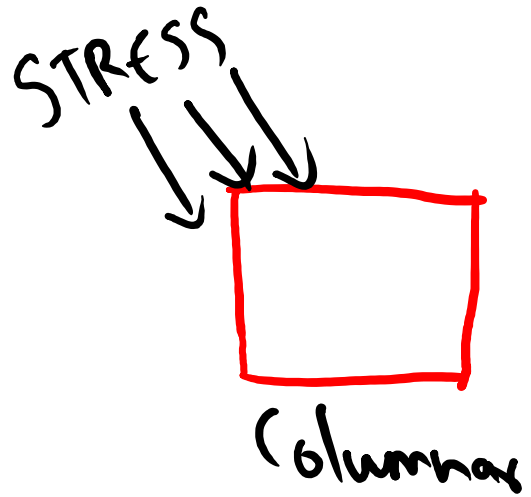
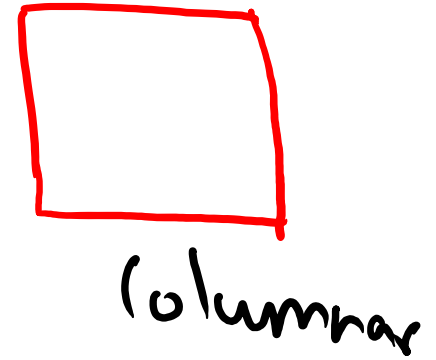


# DEFINITION

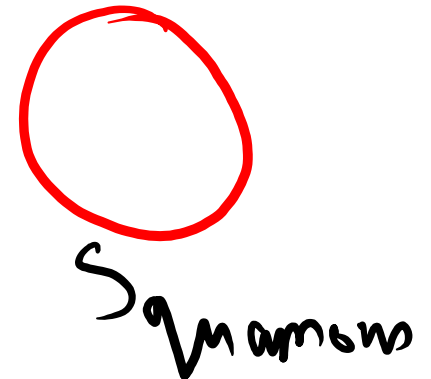
- A reversible change in which **one mature/adult cell type is replaced by another mature/adult cell type**
- If injury or stress abates, the metaplastic tissue may revert to its original type



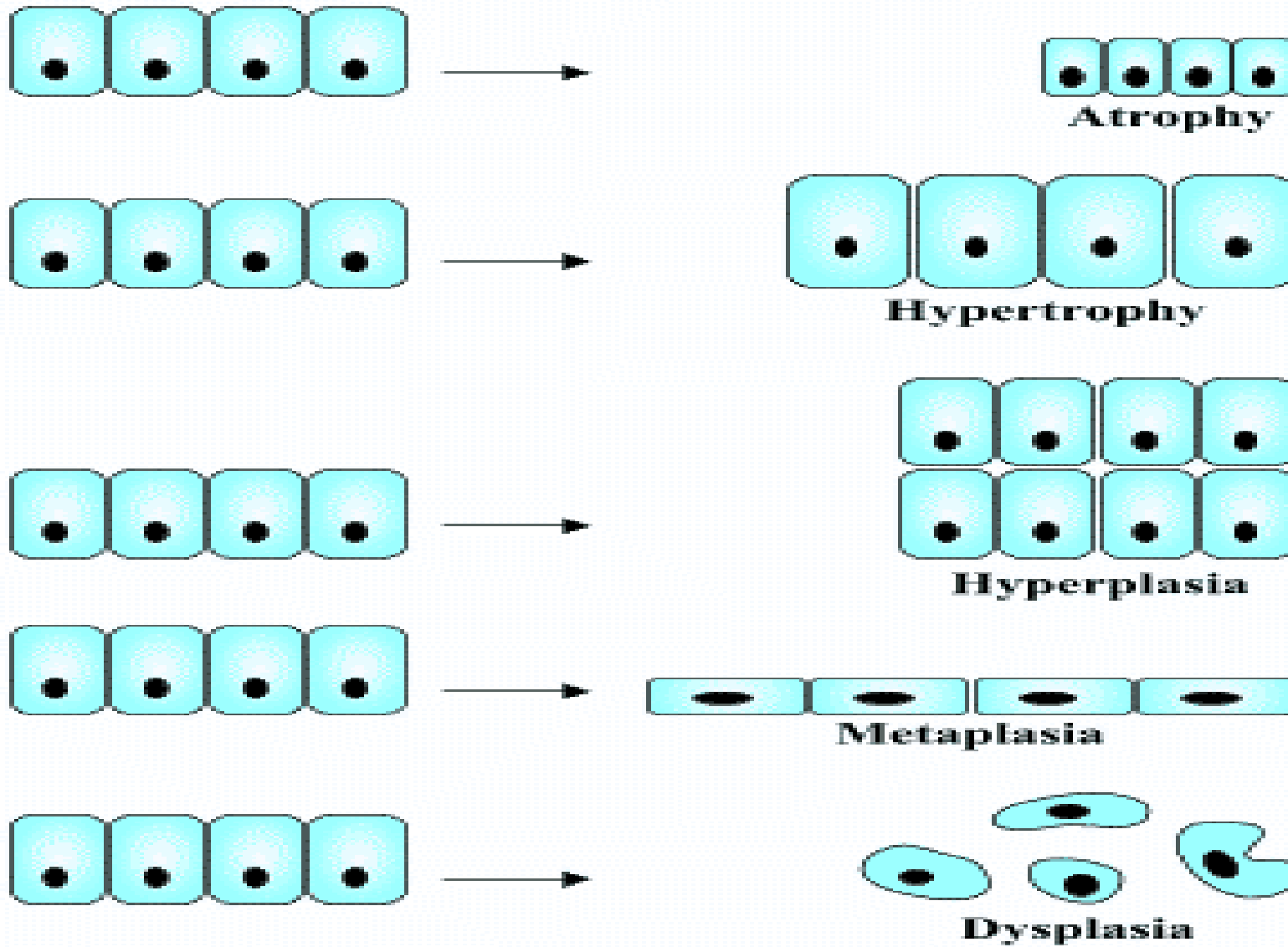
A daptation



Adaptation

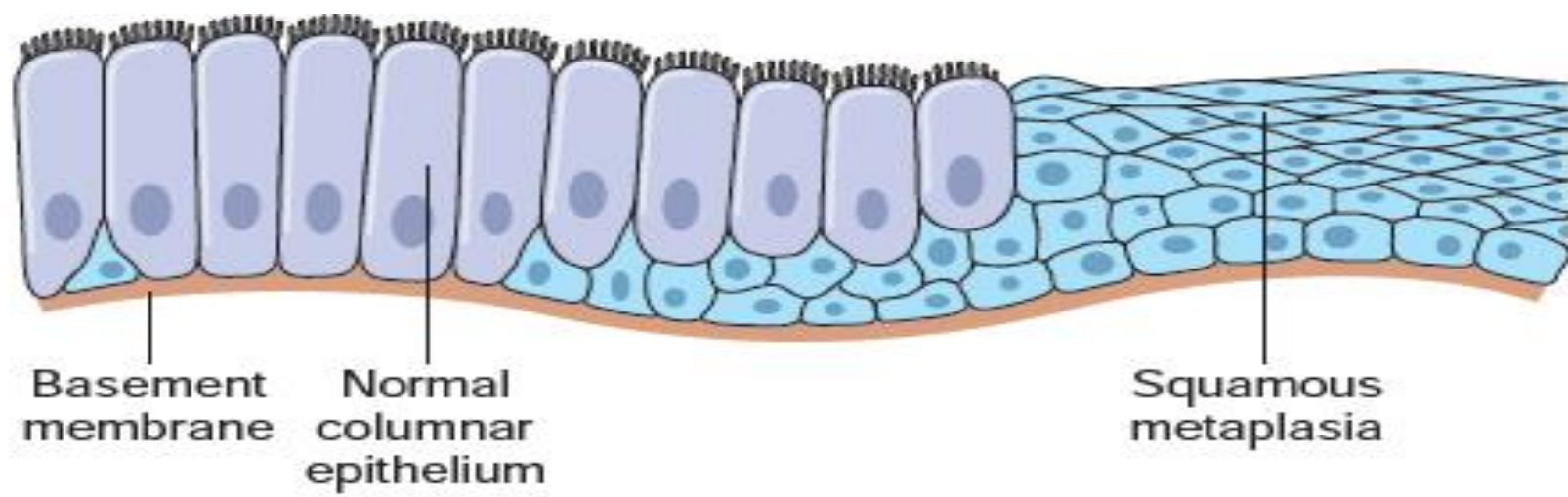


## Cellular Adaptation to Stress

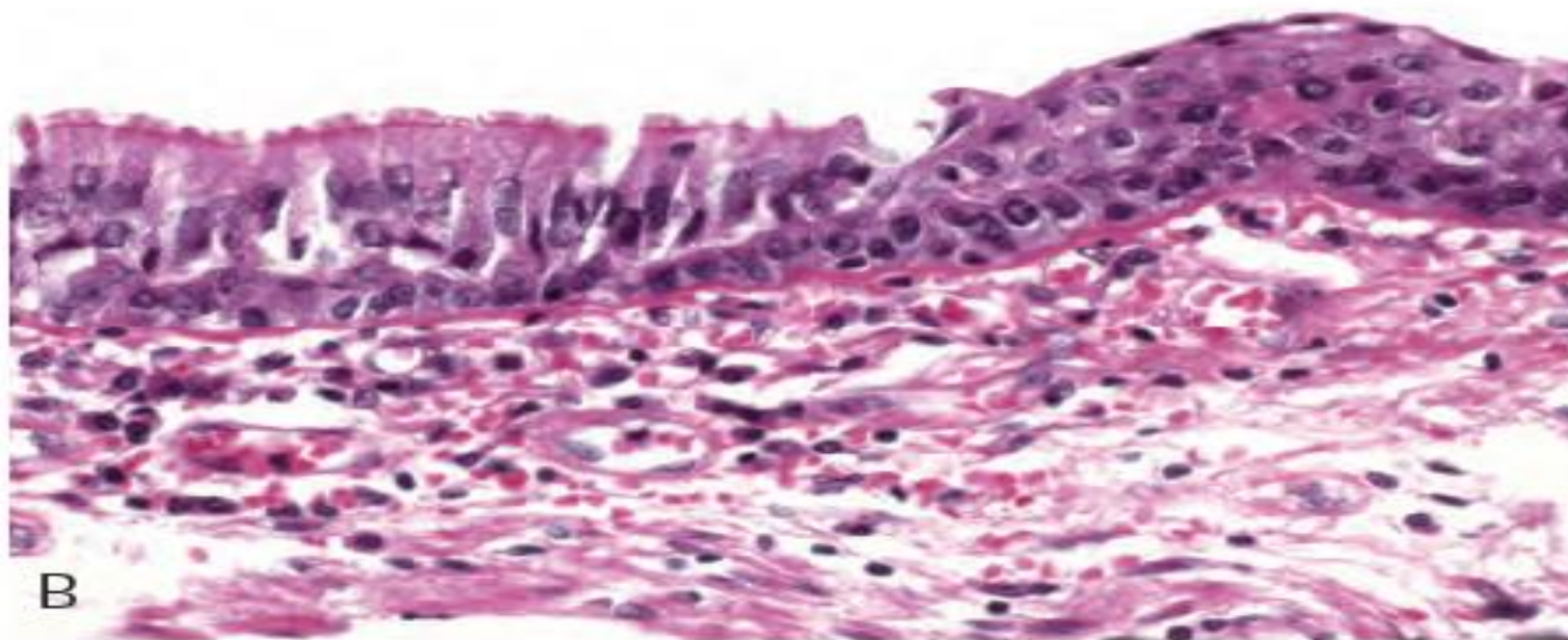


# Mechanisms

- Metaplasia does not result from a change in the phenotype of an already differentiated cell type;
- Metaplasia is the result of a **reprogramming of stem cells that are known to exist in normal tissues.**



A



B



# Headings

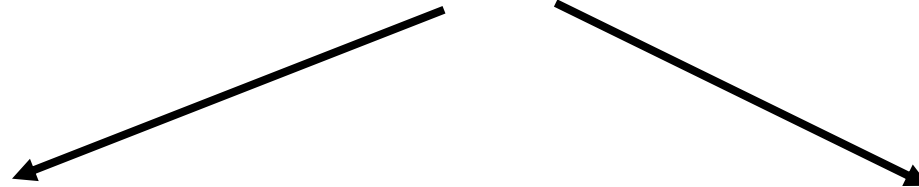
- **Defination**
- **Diagram**
- **Mechanism**
- **Types with examples**
- **Morphology**

# **METAPLASIA**



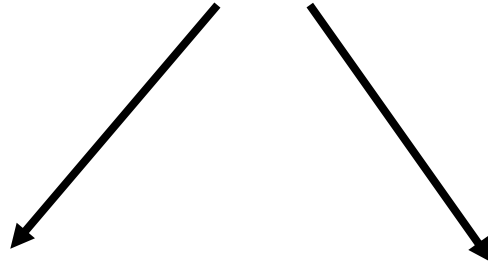
```
graph TD; A[METAPLASIA] --> B[EPITHELIAL]; A --> C[MESENCHYMAL]; B --> D[SQUAMOUS]; B --> E[COLUMNAR]; C --> F[OSSEOUS]; C --> G[CARTILAGINOUS]
```

A hierarchical flowchart showing the classification of metaplasia. The root node is 'METAPLASIA', which branches into 'EPITHELIAL' and 'MESENCHYMAL'. 'EPITHELIAL' further branches into 'SQUAMOUS' and 'COLUMNAR'. 'MESENCHYMAL' further branches into 'OSSEOUS' and 'CARTILAGINOUS'. All text is in bold black uppercase letters, and arrows indicate the flow from parent to child nodes.



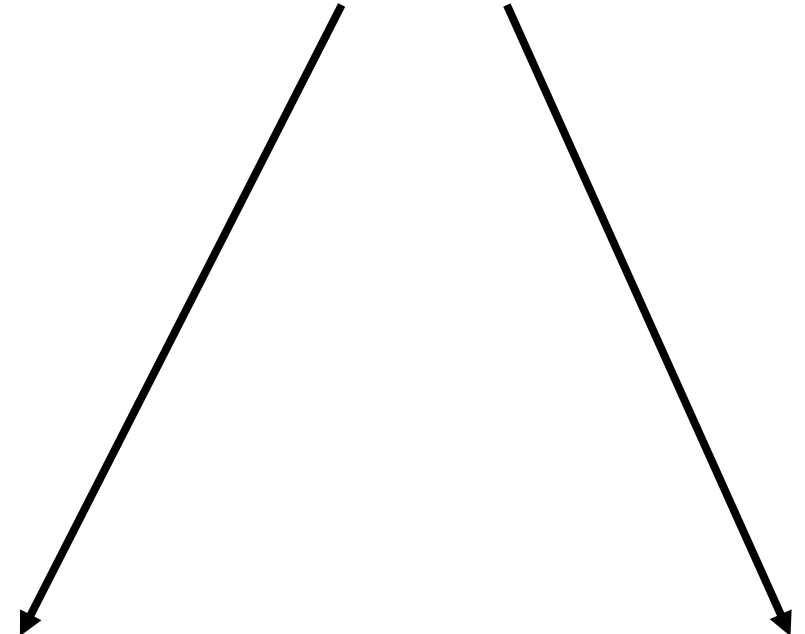
## **EPITHELIAL**

## **MESENCHYMAL**



**SQUAMOUS**

**COLUMNAR**



**OSSEOUS**

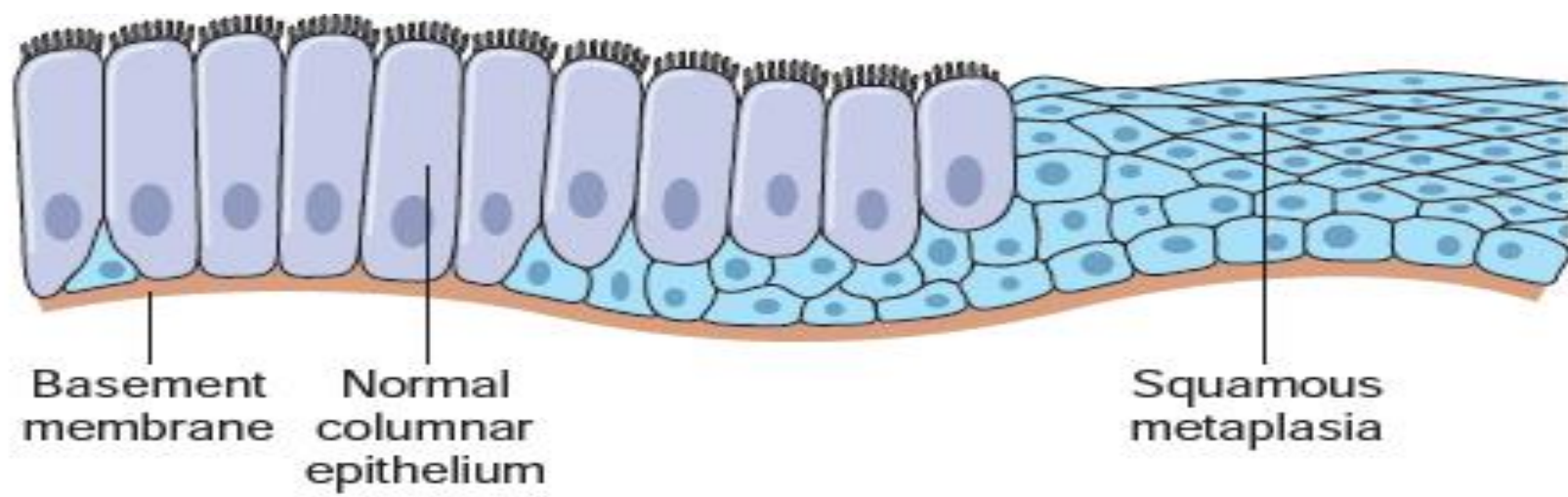
**CARTILAGINOUS**

# EPITHELIAL METAPLASIA

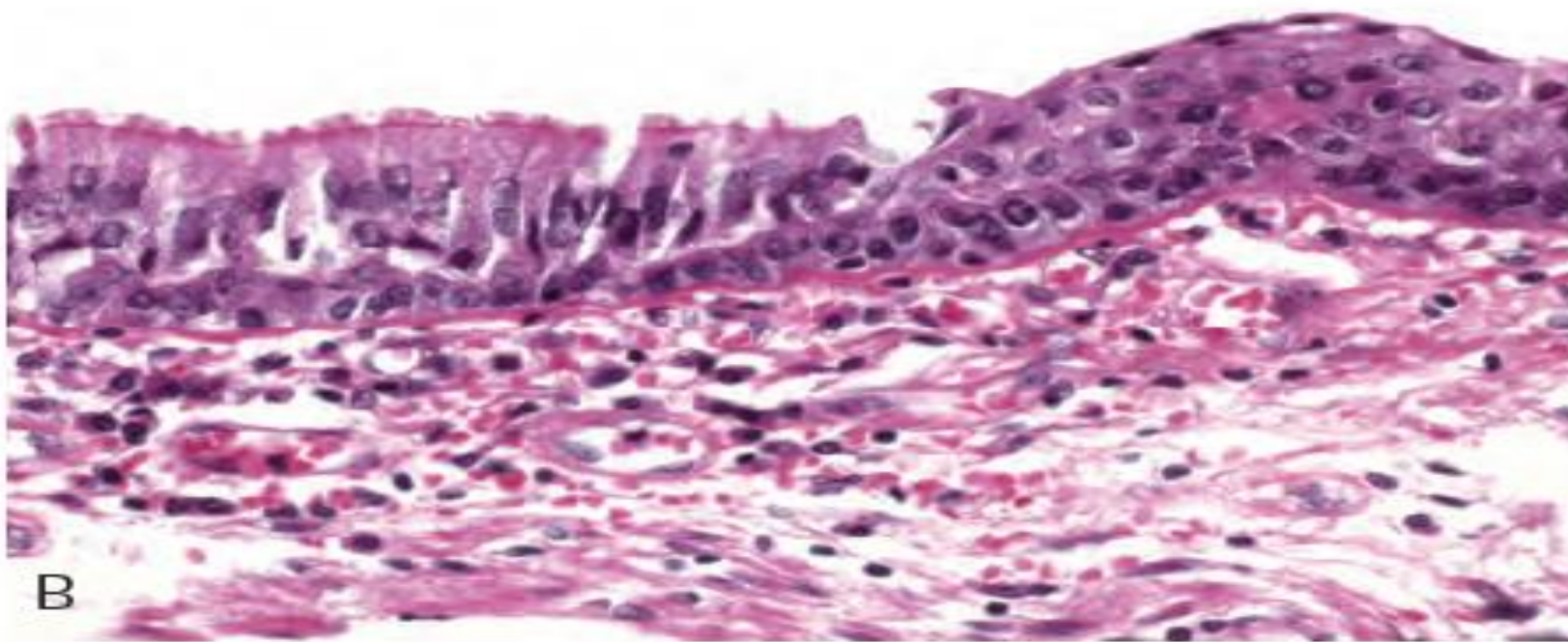
- This is the **more common type**
- Replacement of **one epithelium by stronger but less well specialised epithelium**

# **Squamous metaplasia**

**Normal columnar epithelium → squamous epithelium**



A



B

# EXAMPLES

1. In **bronchus** (normally lined by pseudostratified columnar ciliated epithelium) in chronic smokers.
2. In **uterine endocervix** (normally lined by simple columnar epithelium) in prolapse of the uterus

3. In **gallbladder** (normally lined by simple columnar epithelium) in cholelithiasis.

4. In **prostate** (normally lined by simple columnar epithelium) in chronic prostatitis

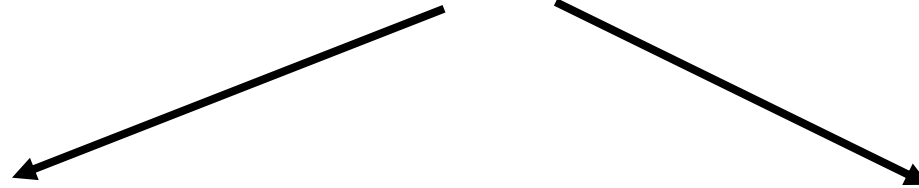
5. Vitamin A deficiency , squamous metaplasia in the **nose, bronchi, lacrimal and salivary glands.**

# **METAPLASIA**



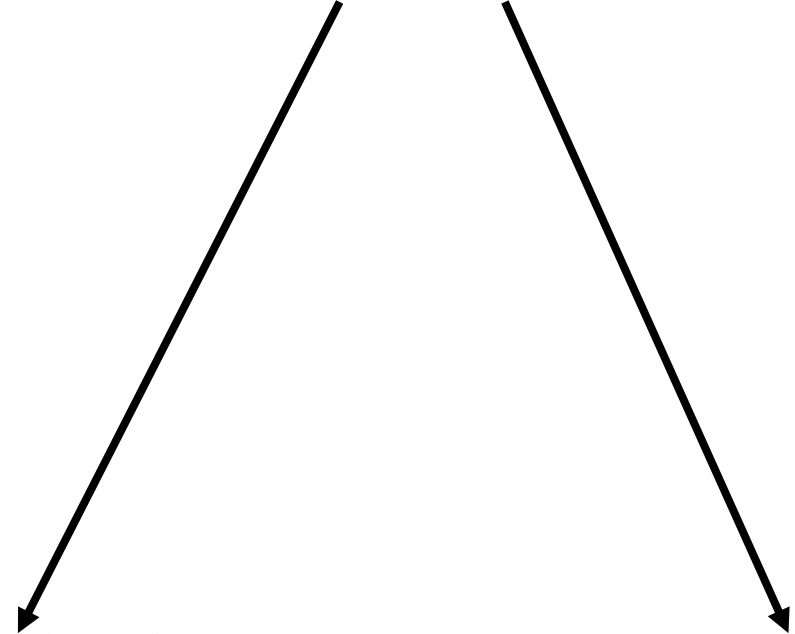
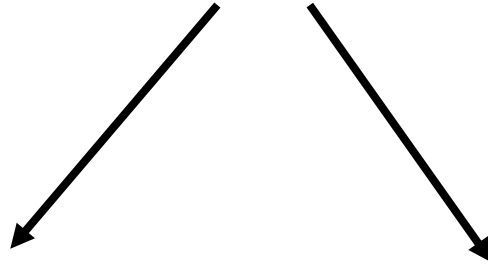
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## **EPITHELIAL**

## **MESENCHYMAL**



**SQUAMOUS**

**COLUMNAR**

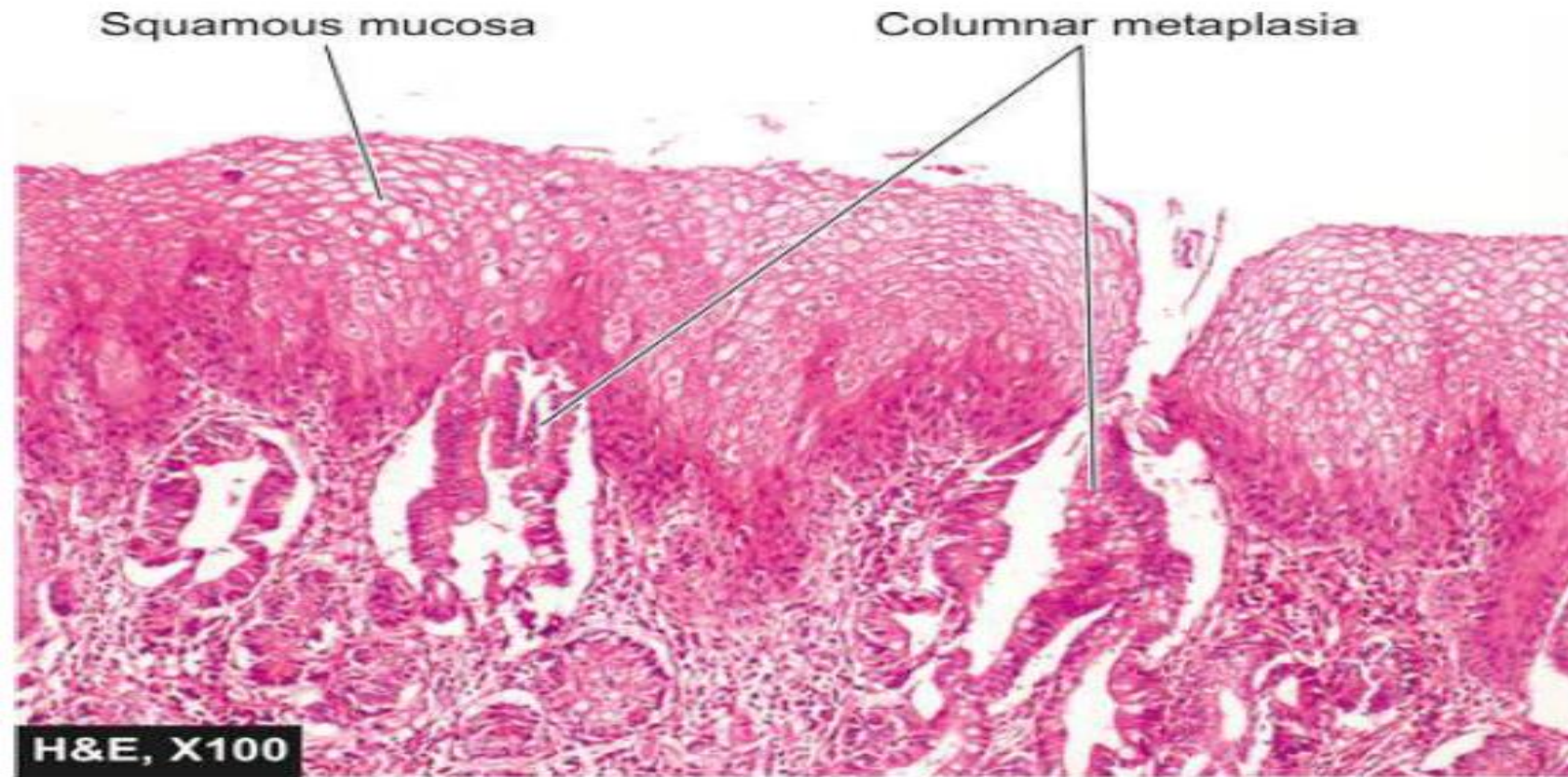
**OSSEOUS**

**CARTILAGINOUS**



# **Columnar metaplasia**

- Normal squamous epithelium → columnar epithelium



**Figure 2.41** Columnar metaplasia oesophagus (Barrett's oesophagus). Part of the oesophagus which is normally lined by squamous epithelium undergoes metaplastic change to columnar epithelium of intestinal type.

# EXAMPLES

1. **Barrett's oesophagus** → change of normal squamous epithelium to columnar epithelium
2. **Cervical erosion** → change of normal squamous epithelium to columnar epithelium

# **METAPLASIA**



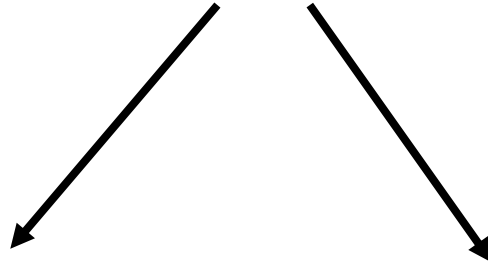
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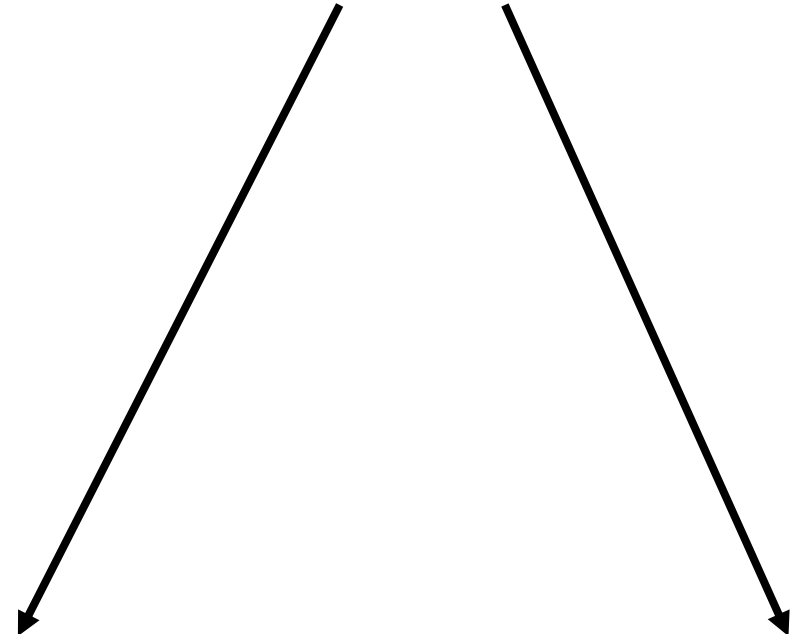
## **EPITHELIAL**

## **MESENCHYMAL**



**SQUAMOUS**

**COLUMNAR**



**OSSEOUS**

**CARTILAGINOUS**

# MESENCHYMAL METAPLASIA

- Less common
- There is transformation of **one adult type of mesenchymal tissue to another ie.** formation of cartilage, bone or adipose tissue (mesenchymal tissues) in tissues that normally do not contain these elements.

# Osseous metaplasia

1. In arterial wall in old age (**Mönckeberg's medial calcific sclerosis**)
2. **Myositis ossificans**
3. In cartilage of **larynx and bronchi** in elderly people
4. In **scar of chronic inflammation** of prolonged duration

# Cartilaginous metaplasia

1. In **healing of fractures**, cartilaginous metaplasia may occur where there is undue mobility.

# 5 TYPES OF ADAPTATIONS

1. **Hypertrophy** → Increase in the size of cells
2. **Hyperplasia** → Increased number of cells
3. **Atrophy** → Decrease in the size of cells / shrinkage of cells
4. **Metaplasia** → Transformation or replacement of one adult cell type with another
5. **Dysplasia** → means 'disordered cellular development'



# DYSPLASIA



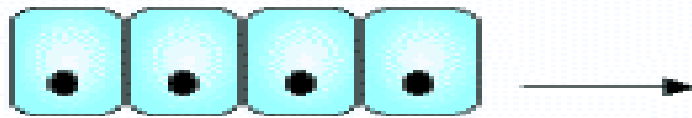
# DYSPLASIA

- Disordered cellular development
- Characterised by cellular cytologic changes

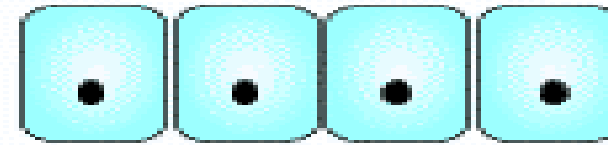
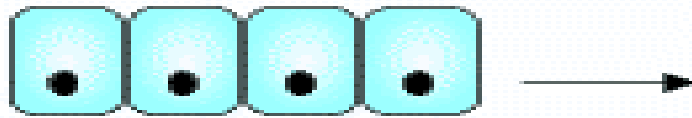
follow us



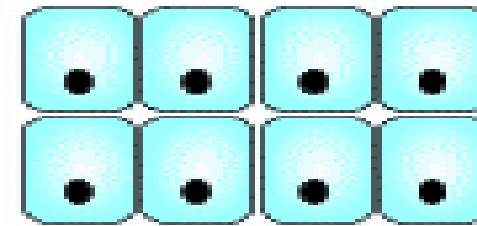
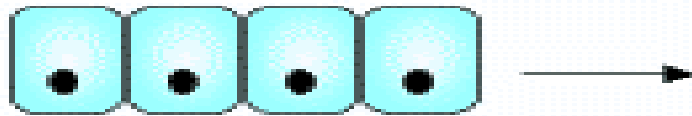
## Cellular Adaptation to Stress



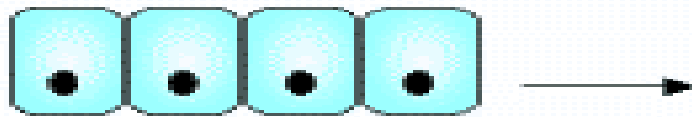
**Atrophy**



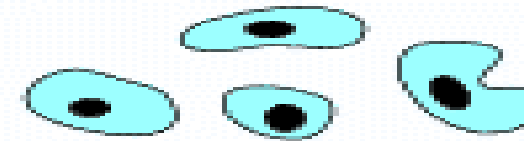
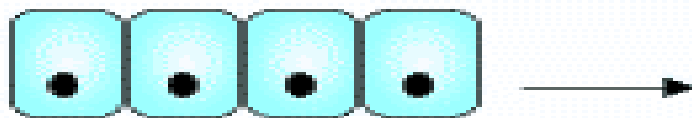
**Hypertrophy**



**Hyperplasia**



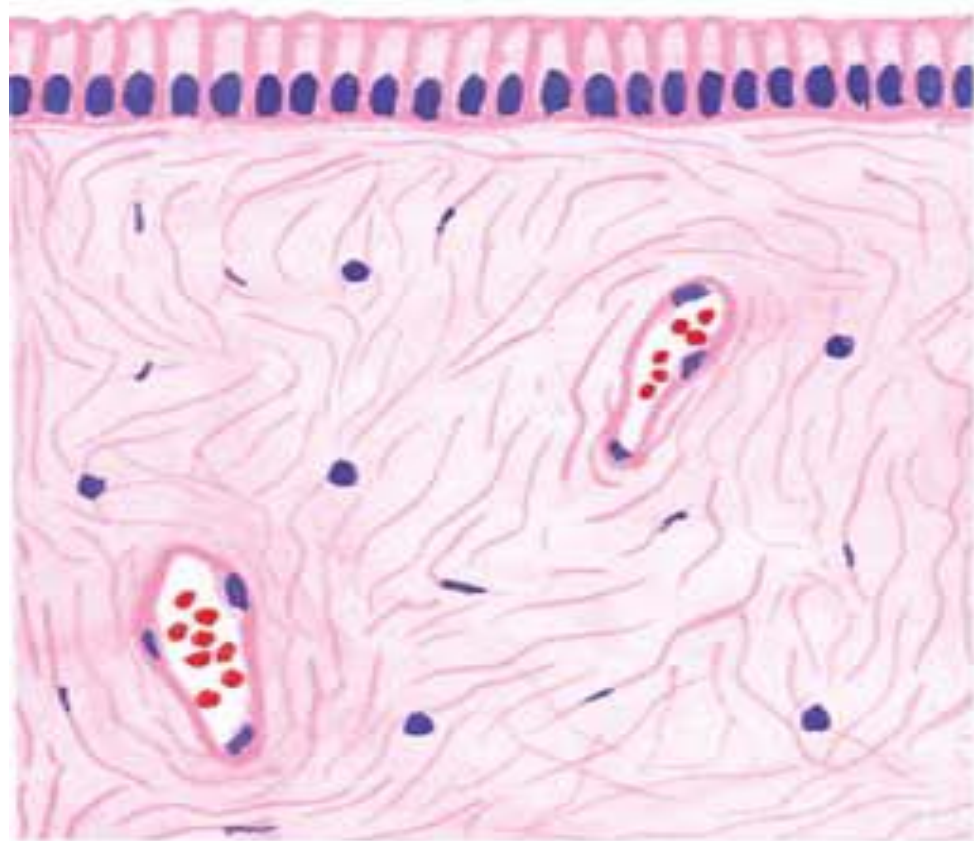
**Metaplasia**



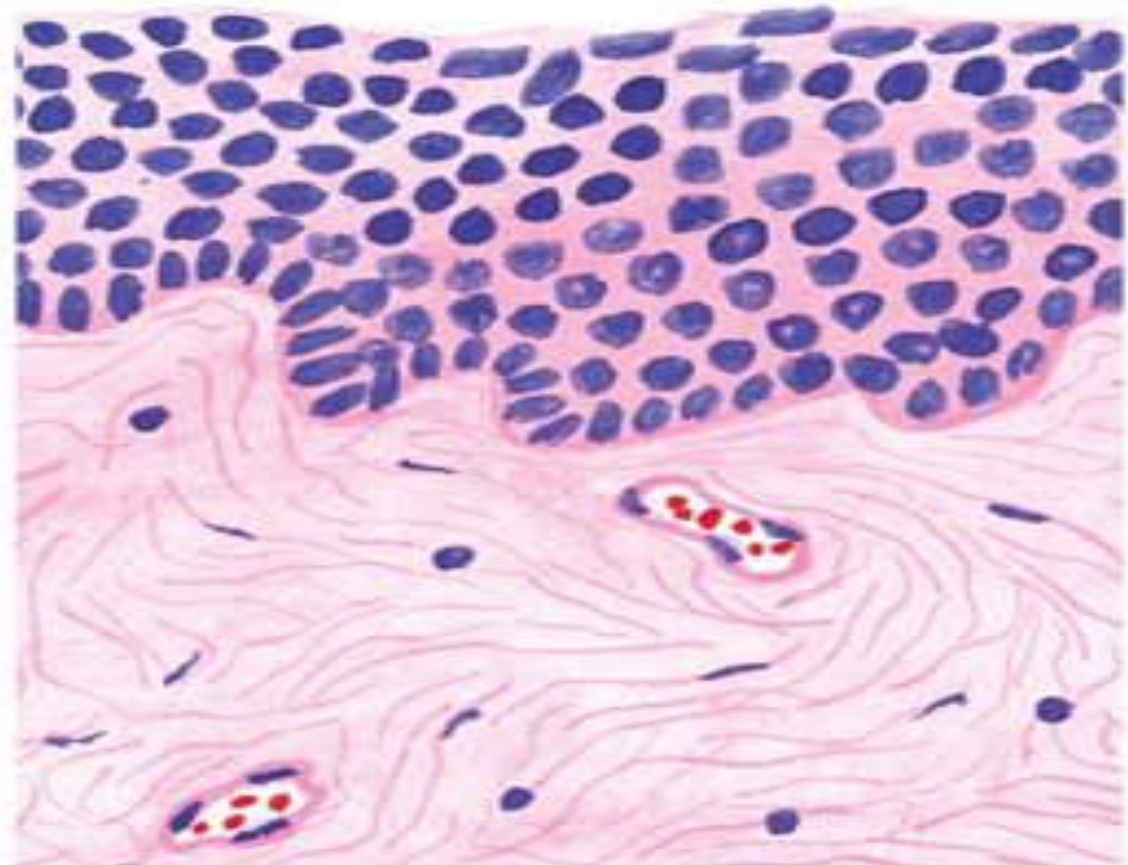
**Dysplasia**

# Cytological changes

1. Increased **number of layers**
2. **Disorderly arrangement** of cells from basal layer to surface layer
3. **Loss of basal polarity** i.e. nuclei lying away from basement membrane
4. Cellular and nuclear **pleomorphism**
5. Increased nucleocytoplasmic **(N/C)** ratio
6. Nuclear **hyperchromatism**
7. Increased **mitotic activity**

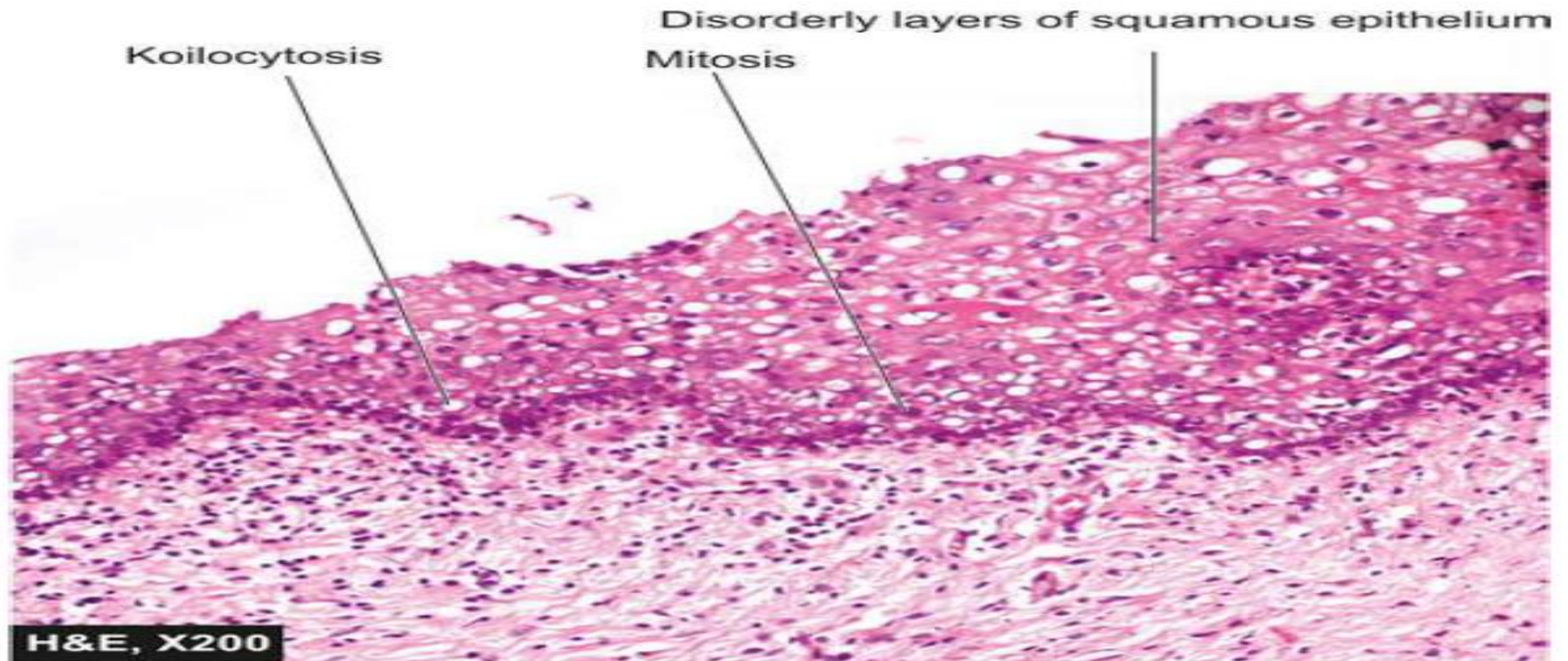


A, NORMAL ENDOCERVICAL  
EPITHELIUM



C, DYSPLASIA



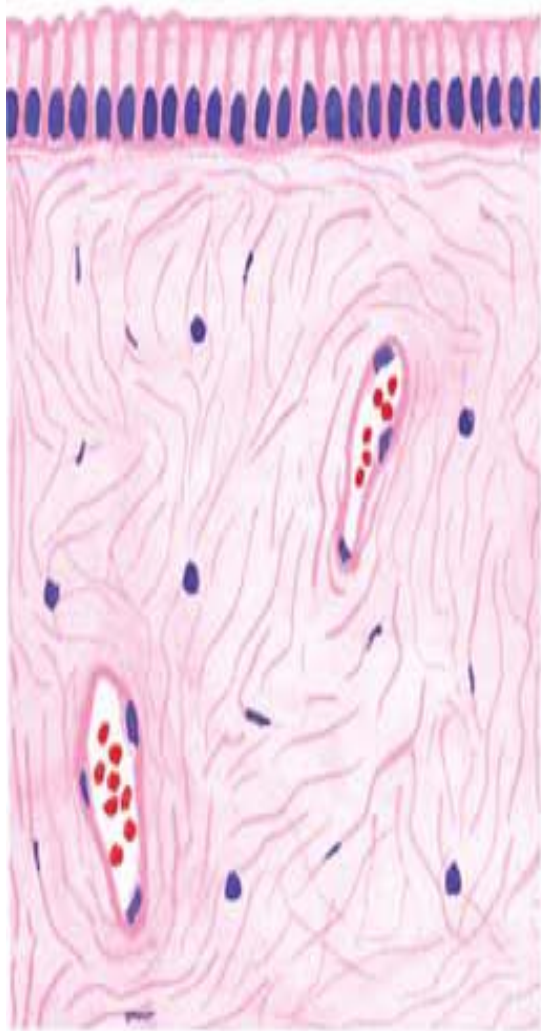


**Figure 2.42** Uterine cervical dysplasia, high grade lesion. It shows increased number of layers of squamous epithelium having marked cytologic atypia including mitoses.

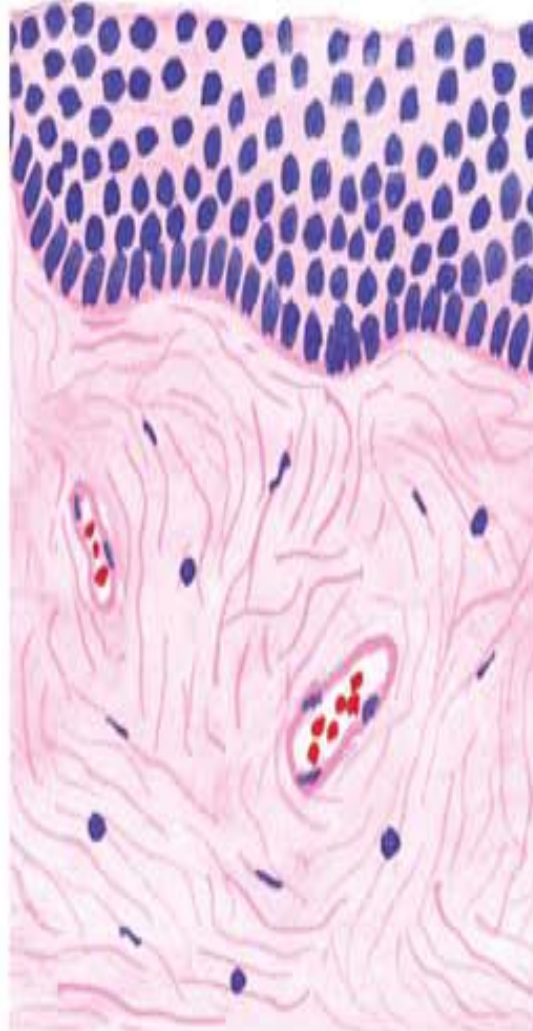
- On removal of stimulus, the changes may disappear.
- Sometimes dysplasia may progress into **carcinoma in situ or invasive cancer.**

FEATURE	METAPLASIA	DYSPLASIA
i) <i>Definition</i>	Change of one type of epithelial or mesenchymal cell to another type of adult epithelial or mesenchymal cell	Disordered cellular development, may be accompanied with hyperplasia or metaplasia
ii) <i>Types</i>	Epithelial (squamous, columnar) and mesenchymal (osseous, cartilaginous)	Epithelial only
iii) <i>Tissues affected</i>	Most commonly affects bronchial mucosa, uterine endocervix; others mesenchymal tissues (cartilage, arteries)	Uterine cervix, bronchial mucosa
iv) <i>Cellular changes</i>	Mature cellular development	Disordered cellular development (pleomorphism, nuclear hyperchromasia, mitosis, loss of polarity)
v) <i>Natural history</i>	Reversible on withdrawal of stimulus	May regress on removal of inciting stimulus, or may progress to higher grades of dysplasia or carcinoma <i>in situ</i>

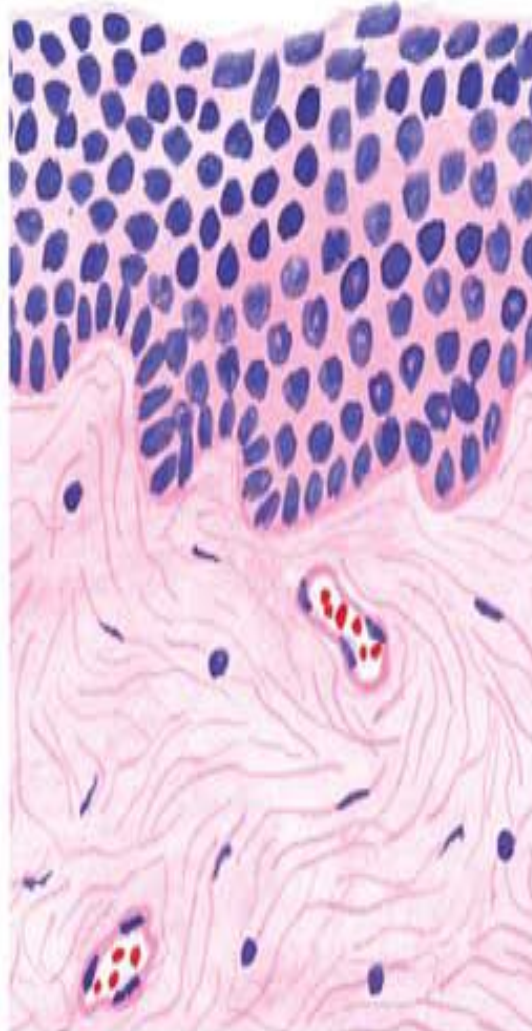




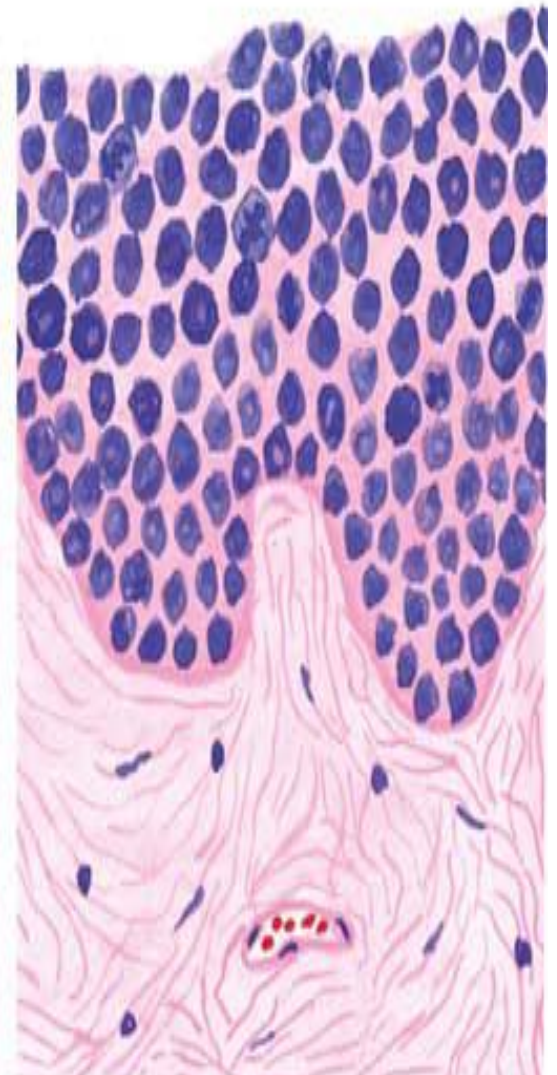
A, NORMAL ENDOCERVICAL  
EPITHELIUM



B, SQUAMOUS METAPLASIA



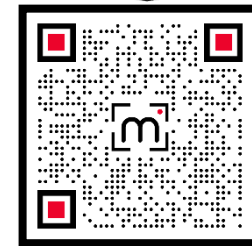
C, DYSPLASIA



D, CARCINOMA *IN SITU*

# QUICK REVISION

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Telegram group discussion*



HYPERPLASIA



HYPERTROPHY



ATROPHY



METAPLASIA



DYSPLASIA



# 5 TYPES OF ADAPTATIONS

1. **Hypertrophy** → Increase in the size of cells
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3. **Atrophy** → Decrease in the size of cells / shrinkage of cells
4. **Metaplasia** → Transformation or replacement of one adult cell type with another
5. **Dysplasia** → means 'disordered cellular development'

# POLLS 1

*Scan or Click to watch  
Cell Adaptation & Injury*



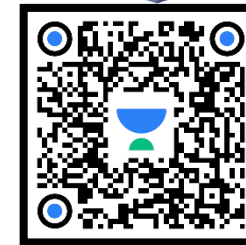
*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*

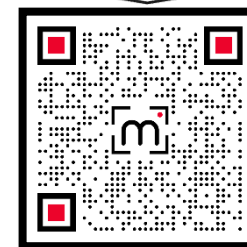


**Both hyperplasia and hypertrophy are seen in?**

- (a) Breast enlargement during lactation
- (b) Uterus during pregnancy
- (c) Skeletal muscle enlargement during exercise
- (d) Left ventricular hypertrophy during heart failure

# B

 *Click or Scan QR code to join  
Telegram group discussion*



**Transformation of one epithelium to other epithelium is known as:**

- |               |                 |
|---------------|-----------------|
| (a) Dysplasia | (b) Hyperplasia |
| (c) Neoplasia | (d) Metaplasia  |



**D**

**All are true about metaplasia except:**

- (a) Slow growth
- (b) Reverse back to normal with appropriate treatment
- (c) Irreversible
- (d) If persistent may induce cancer transformation

**C**



FOLLOW US

**About hyperplasia, which of the following statement is false?**

- (a) ↑ no of cells
- (b) ↑ size of the affected cell
- (c) Endometrial response to estrogen is an example
- (d) All

**B**

An old man Muthoot has difficulty in urination associated with increased urge and frequency. He has to get up several times in night to relieve himself. There is no history of any burning micturition and lower back pain. On rectal examination, he has enlarged prostate. Which of the following represents the most likely change in the bladder of this patient?

- |                 |                |
|-----------------|----------------|
| (a) Hyperplasia | (b) Atrophy    |
| (c) Hypertrophy | (d) Metaplasia |

**C**



**An increase in the size of a cell in response to stress is called hypertrophy. Which of the following does not represent the example of smooth muscle hypertrophy as an adaptive response to the relevant situation?**

- (a) Urinary bladder in urine outflow obstruction**
- (b) Small intestine in intestinal obstruction**
- (c) Triceps in body-builders**
- (d) None of the above**



**c**

**All are cellular adaptations except**

- a) Hypertrophy
- b) Hyperplasia
- c) Necrosis
- d) Metaplasia

**c**

**In comparison to hyperplasia, hypertrophy involves-**

- a) Increase in cell size and number
- b) Increase in cell size without increase in number
- c) Increase in cell number without increasing in size
- d) Increase in cell size and decrease in number

**B**

**Decrease in cell size refers to -**

- a) Atrophy
- b) Metaplasia
- c) Hyperplasia
- d) Hypertrophy

**A**

# **Examples of metaplasia are the following except-**

- a) Breast enlargement at puberty**
- b) Barrets esophagus**
- c) Myositis Ossificans**
- d) Respiratory tract in chronic smokers**

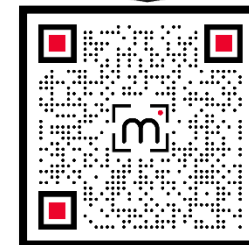


**A**

**CELL ADAPTATIONS**  
**CELL INJURY**  
**CELL DEATH**

# Cell injury

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Telegram group discussion*



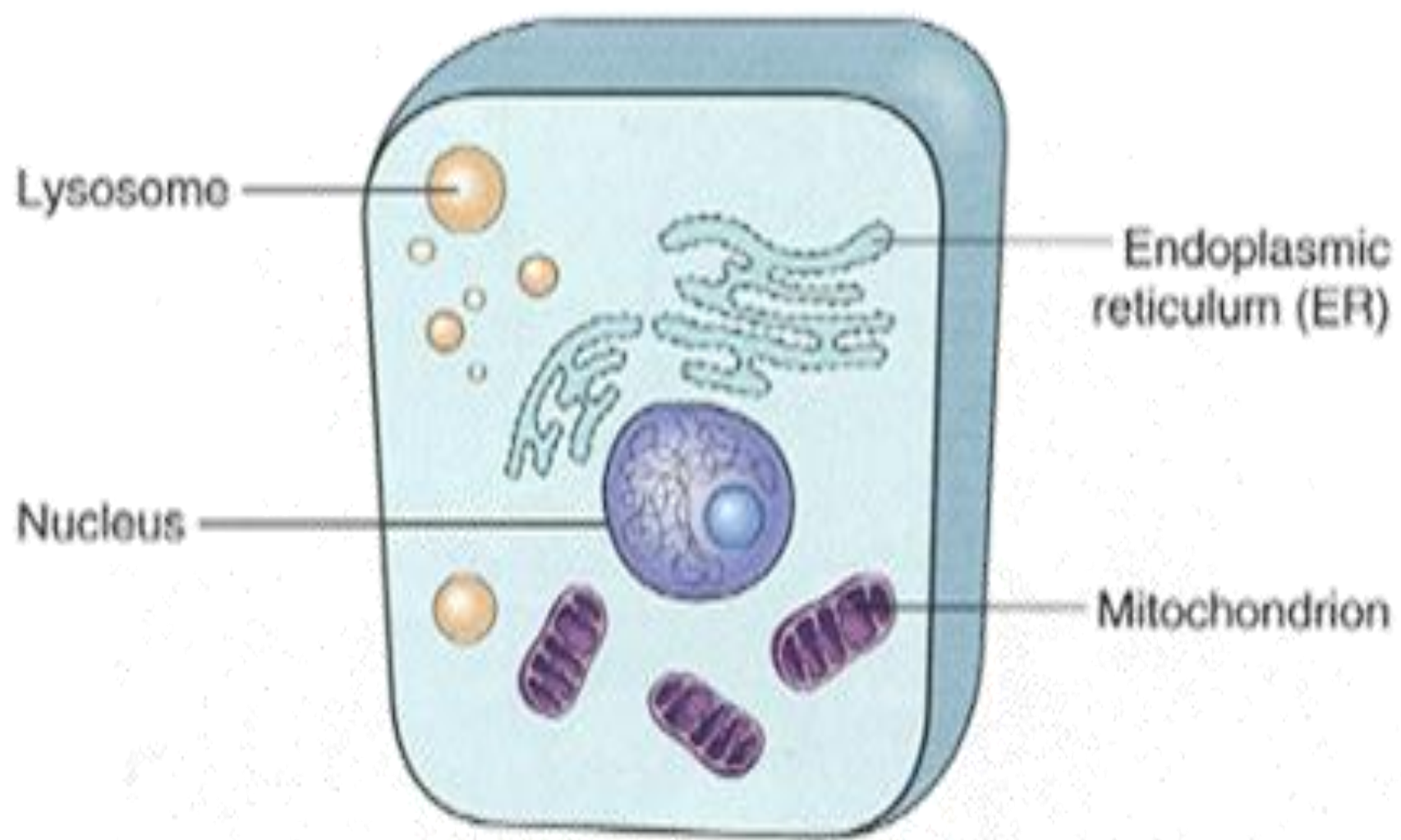
# Headings

- Introduction
- Definition
- Types of cell injury
- Etiology
- Mechanisms → 5
- Morphology

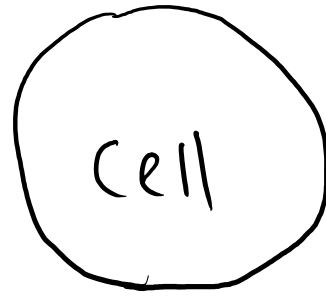
# Introduction

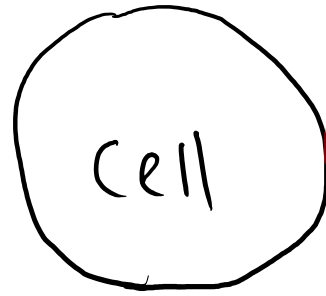
*follow us*





A. Normal cell





STRESS  
(physiological or  
pathological)



**Normally cells in homeostasis**



**Physiological and pathological stress**



**Cellular adaptation** (reversible on withdrawal of stimulus)



**If the irritant stimulus persists for long time**



**Cell injury**



**Reversible cell injury**



**Irreversible cell injury** (Cell death)

**-Apoptosis**

**-Necrosis**

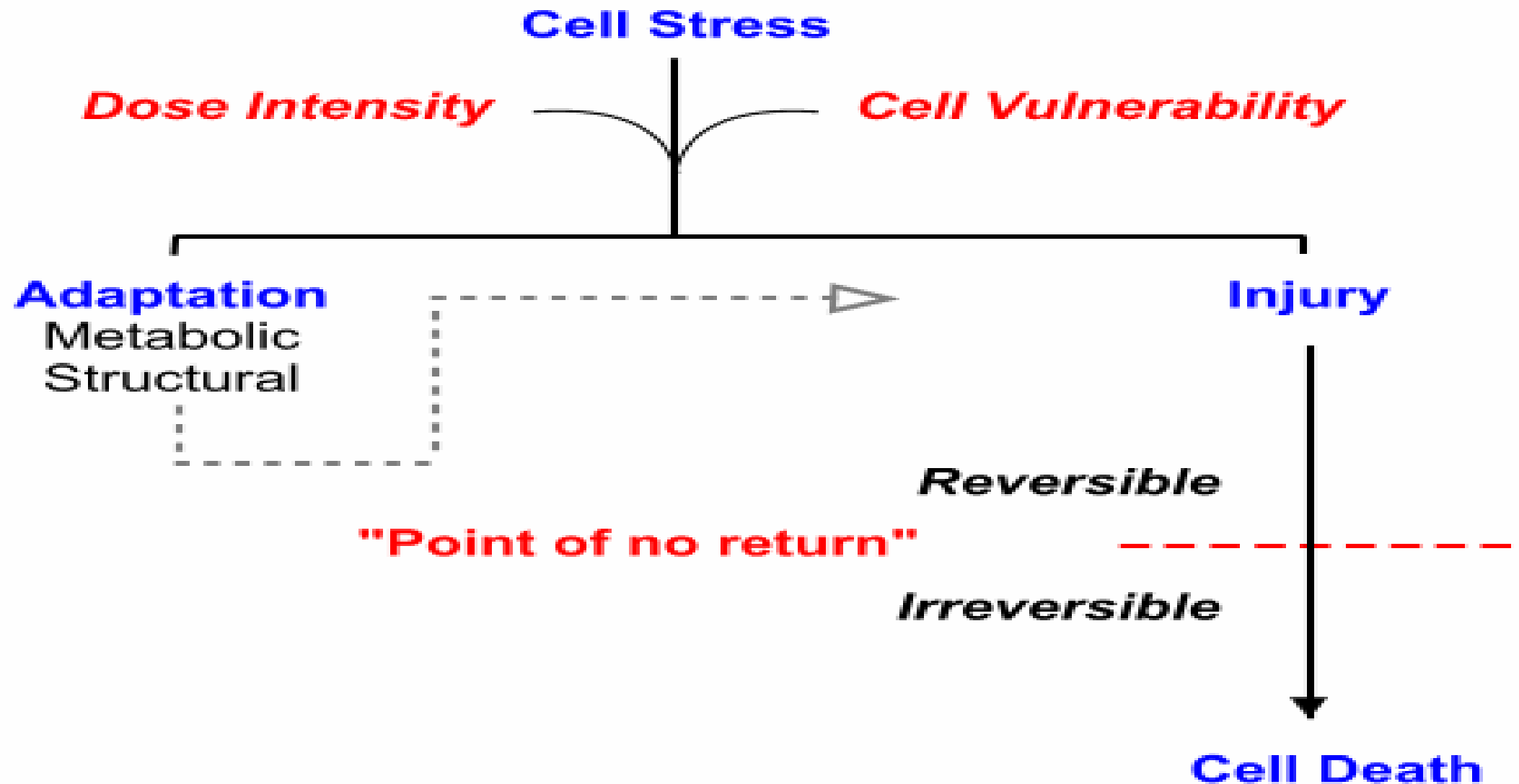
# Headings

- Introduction
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# Cell injury

- Cell injury results **when cells are stressed so severely or persistently that they are no longer able to adapt or when cells are exposed to damaging agents.**

# Cell Injury = Disease



# Headings

- Introduction
- Definition
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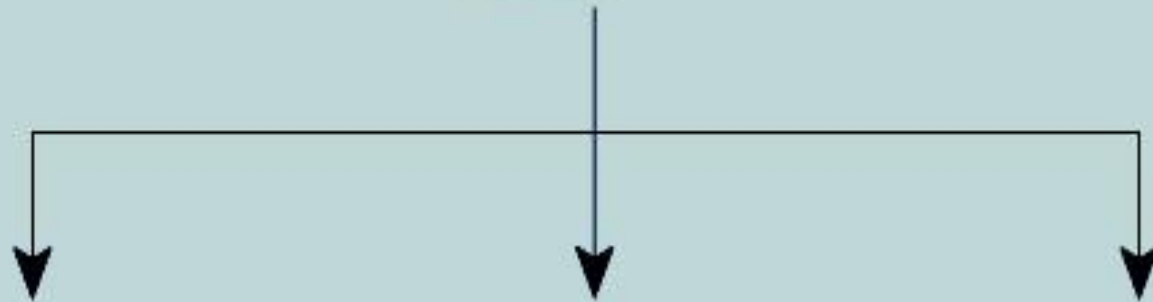
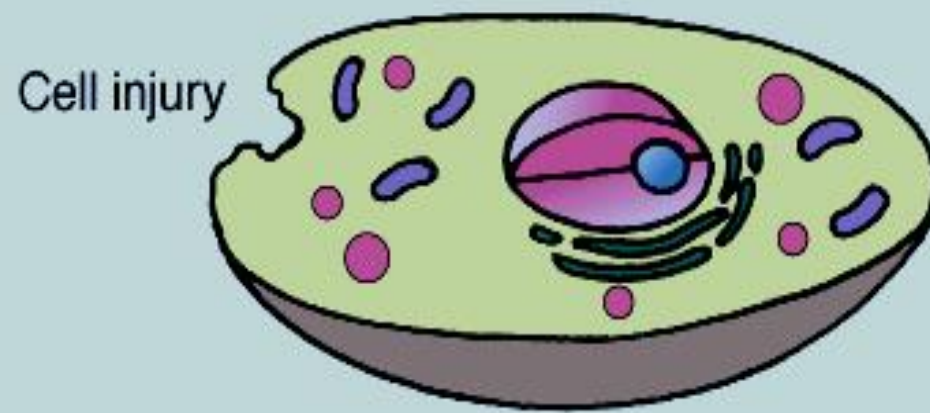
# **TYPES**

- Depending on the type, severity and duration of injury cell injury of 2 types →

## **1. Reversible**

## **2. Irreversible = Cell death**

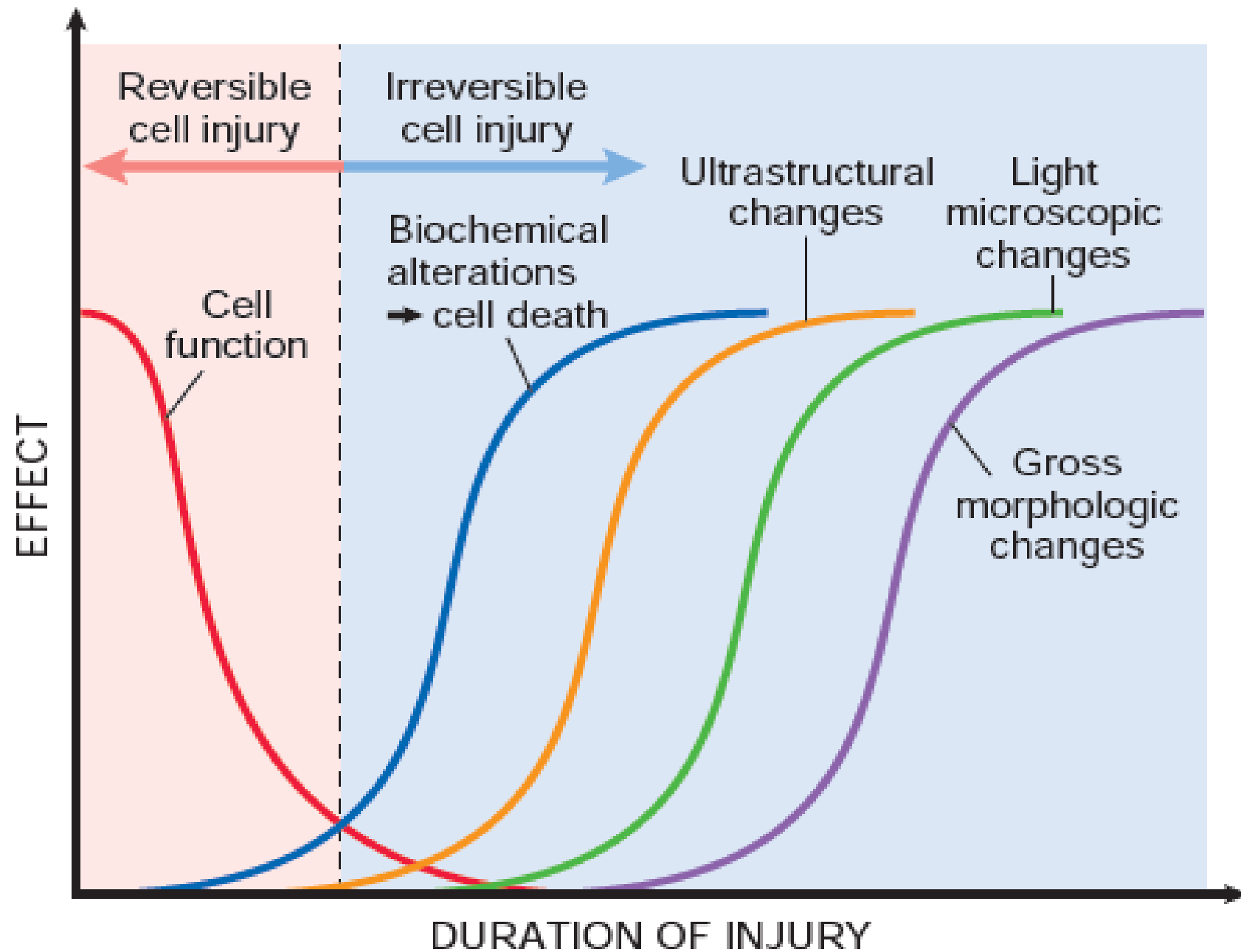
- Necrosis**
- Apoptosis**



Reversible injury,  
cell recovery,  
and return  
to normal function

Apoptosis  
and  
programmed  
cell removal

Cell death  
and  
necrosis





# Headings

- Introduction
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- Mechanisms → 5
- Morphology

# ETIOLOGY

## A. Genetic causes

## B. Acquired causes

- 1. Hypoxia and ischaemia
- 2. Physical agents
- 3. Chemical agents and drugs
- 4. Microbial agents
- 5. Immunologic agents
- 6. Nutritional derangements
- 7. Ageing
- 8. Psychogenic diseases
- 9. Iatrogenic factors
- 10. Idiopathic diseases.

# Headings

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- Morphology

# **Mechanisms of Cell Injury**

**5 mechanisms**→

- 1. ATP depletion**
- 2. Mitochondrial Damage**
- 3. Loss of calcium homeostasis**
- 4. Defects in membrane permeability**
- 5. Free radical injury**

# ATP Depletion

Like us



Ischemia



Mitochondrion



↓ Oxidative phosphorylation

↓ ATP

↓ Na<sup>+</sup> pump

↑ Influx of Ca<sup>2+</sup>  
H<sub>2</sub>O, and Na<sup>+</sup>

↑ Efflux of K<sup>+</sup>

ER swelling  
Cellular swelling  
Loss of microvilli  
Blebs

↑ Anaerobic glycolysis

↓ Glycogen

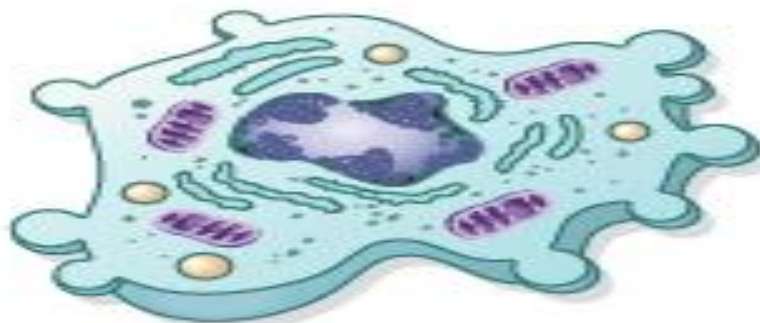
↑ Lactic acid

↓ pH

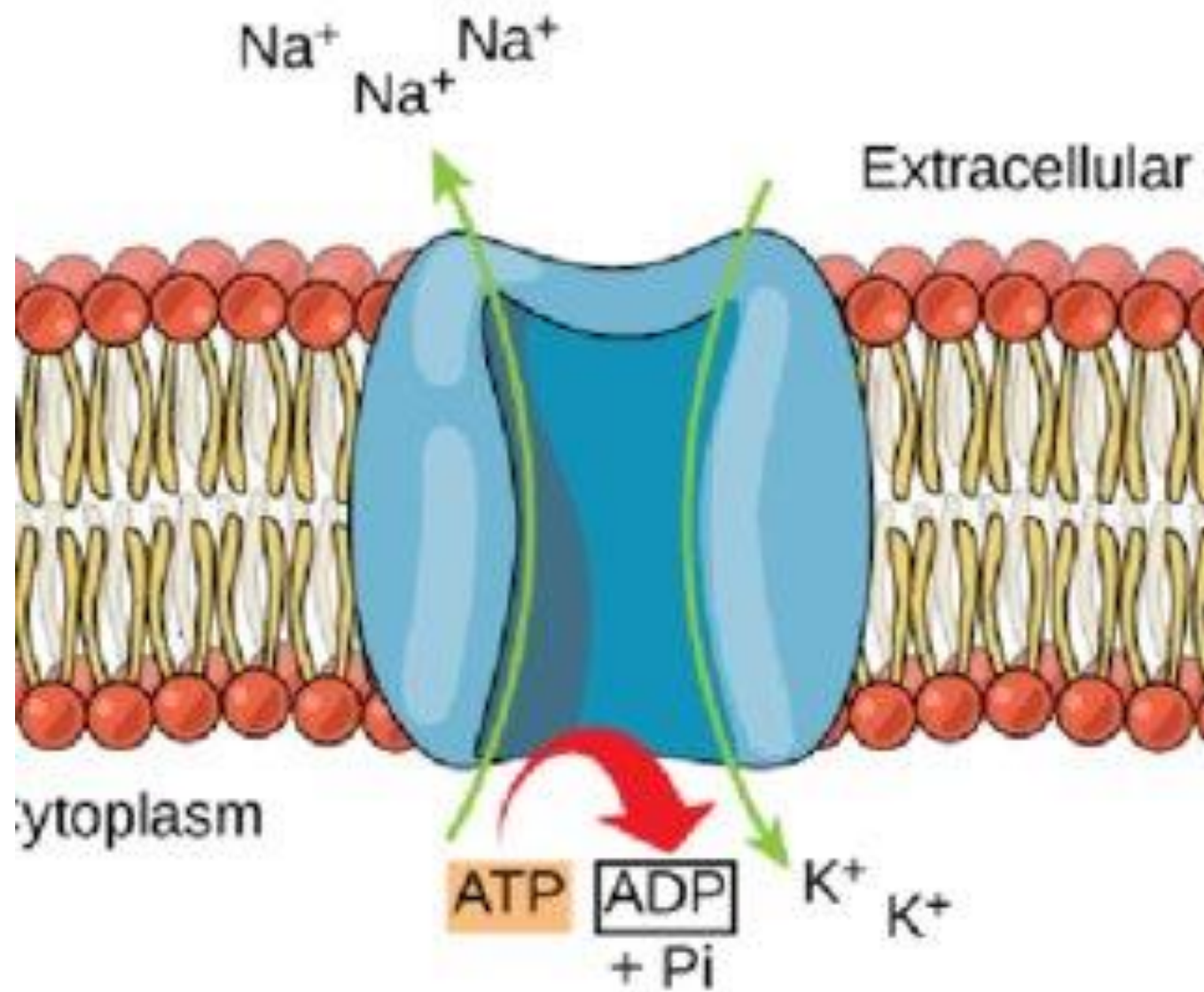
Detachment  
of ribosomes

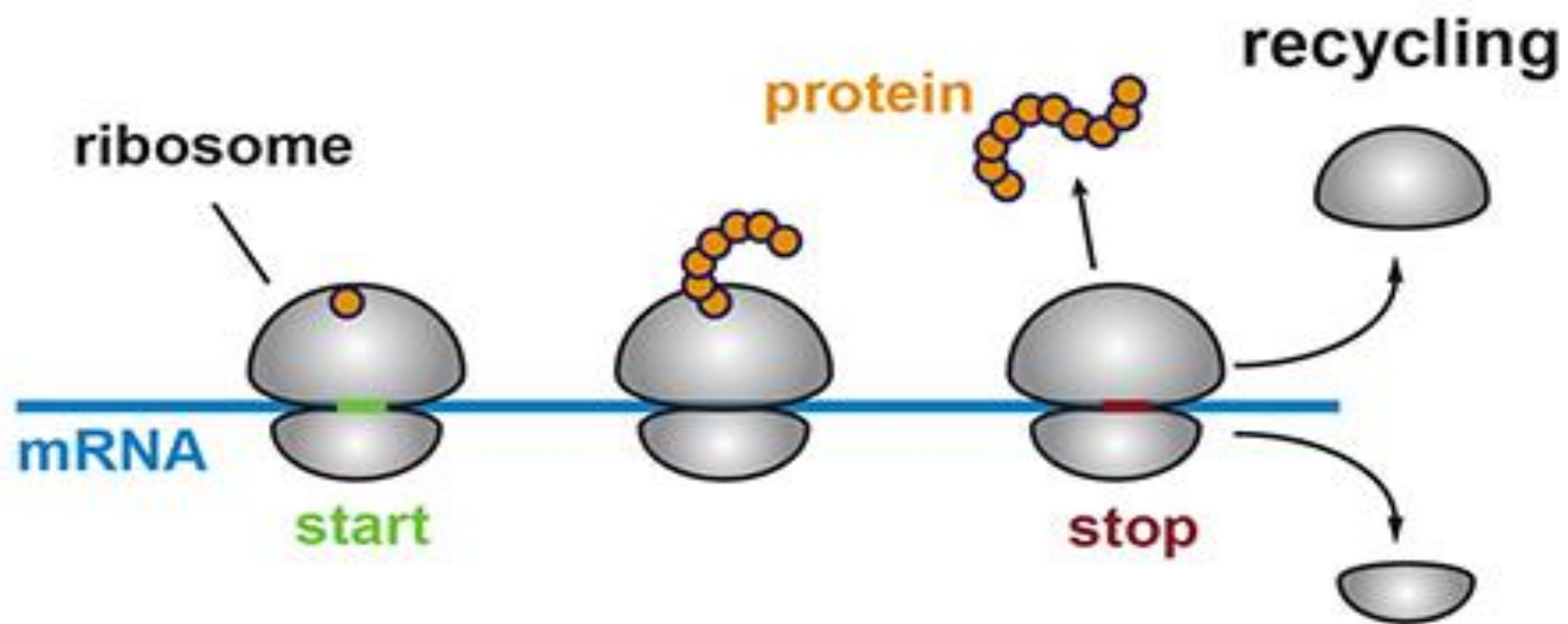
↓ Protein  
synthesis

Clumping of  
nuclear  
chromatin



## Sodium-Potassium Pump







**Ischemic**



**Mitochondria - reduced oxidative phosphorylation.**



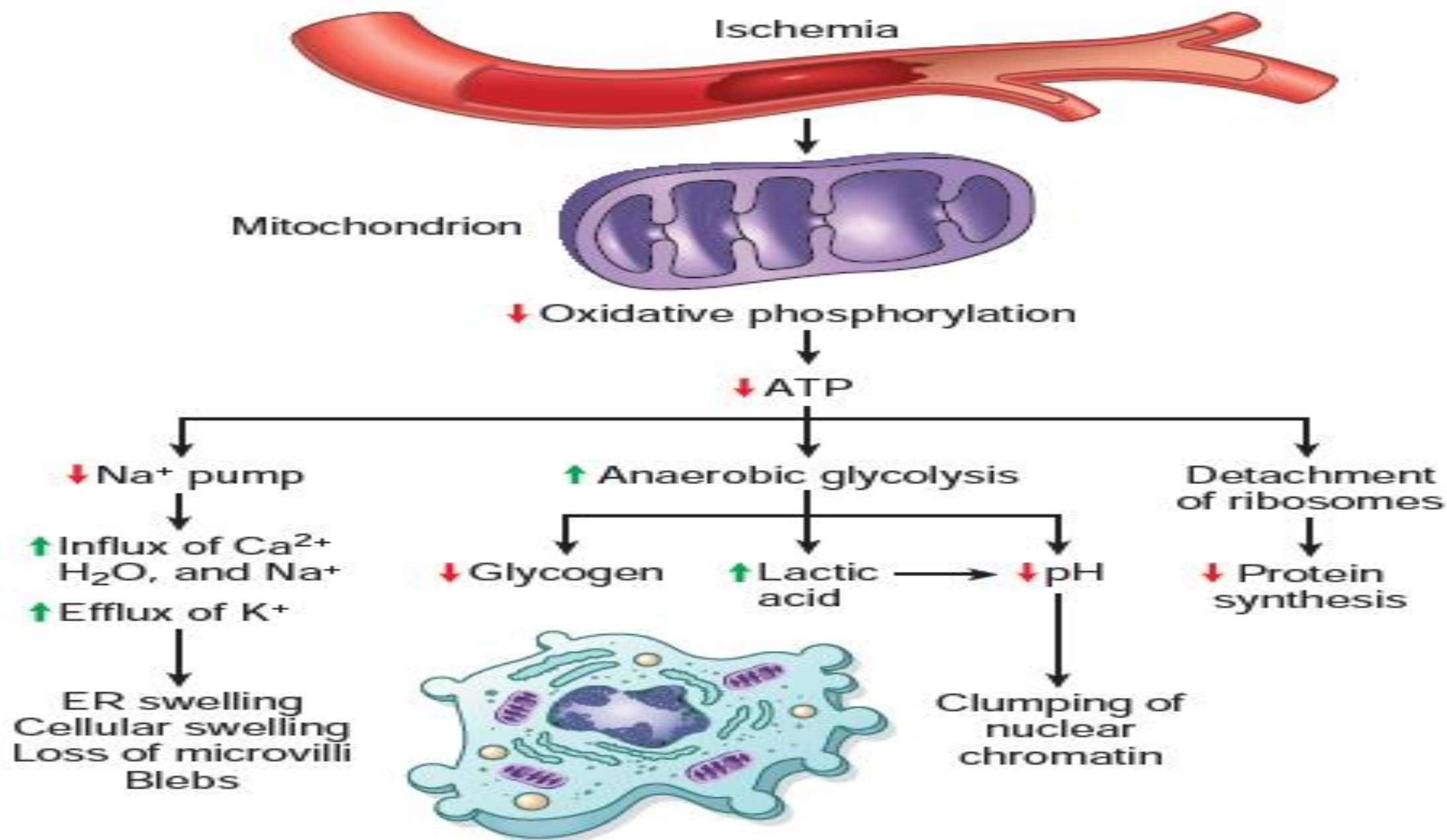
**Cell membrane - reduced sodium pump.**



**Sodium and water enter the cell; potassium exits.**



**Endoplasmic reticulum dilates, the cell swells, blebs appear.**



**Anaerobic glycolysis occurs**



**Loss of glycogen**



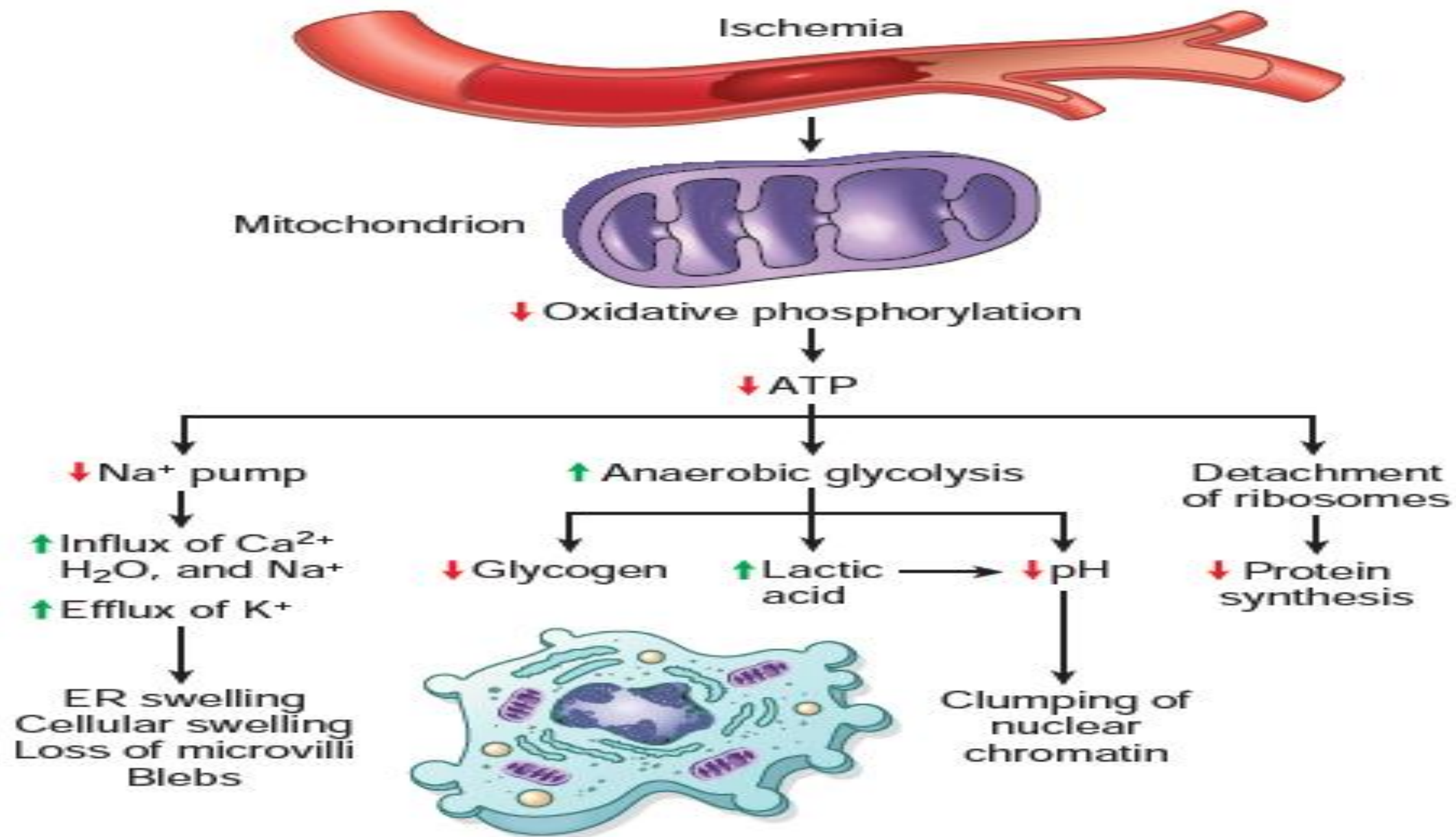
**Accumulation of lactic acid,**



**Acid pH**



**Interferes with enzymes and clumping of nuclear chromatin**



**Decreased ATP**



**RER loses ribosomes**



**Protein synthesis falls**



**Structural proteins (membranes, cytoskeleton) and enzymes  
depletes**



Mitochondrion



↓ Oxidative phosphorylation

↓ ATP

↓ Na<sup>+</sup> pump

↑ Influx of Ca<sup>2+</sup>  
H<sub>2</sub>O, and Na<sup>+</sup>

↑ Efflux of K<sup>+</sup>

ER swelling  
Cellular swelling  
Loss of microvilli  
Blebs

↑ Anaerobic glycolysis

↓ Glycogen

↑ Lactic acid

↓ pH

Detachment  
of ribosomes

↓ Protein  
synthesis

Clumping of  
nuclear  
chromatin



# **Mechanisms of Cell Injury**

**5 mechanisms**→

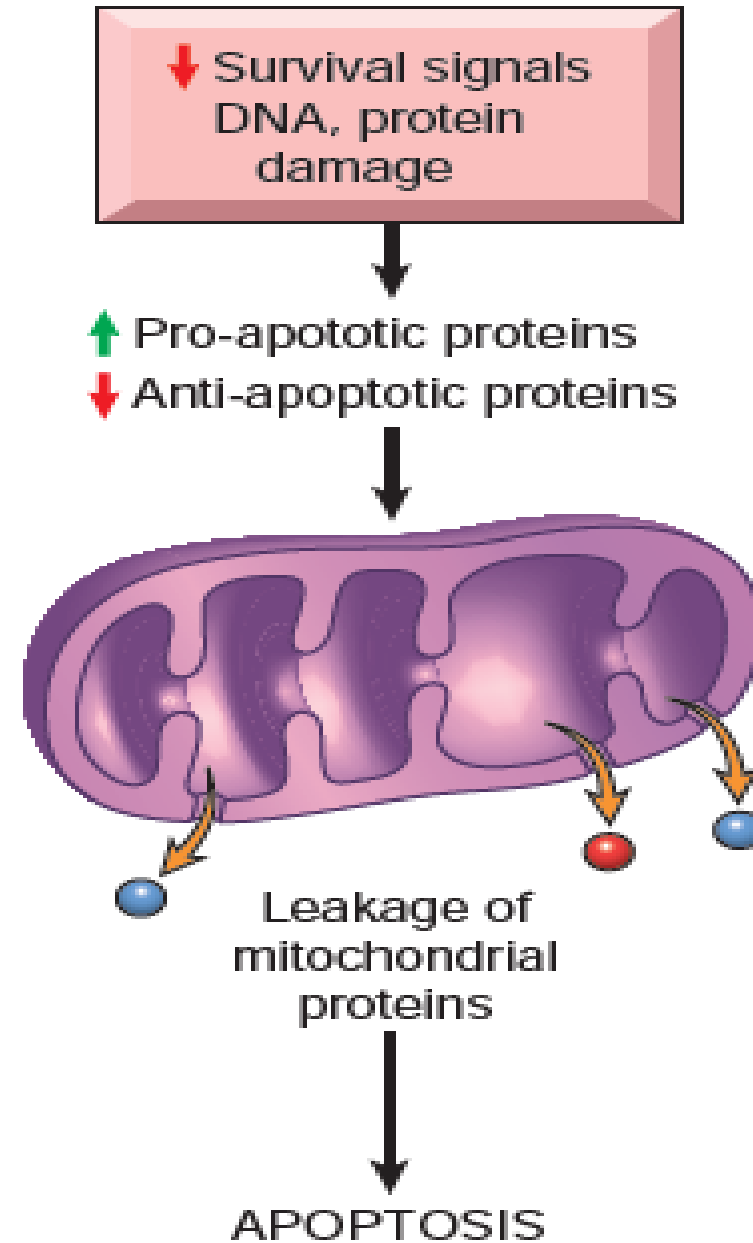
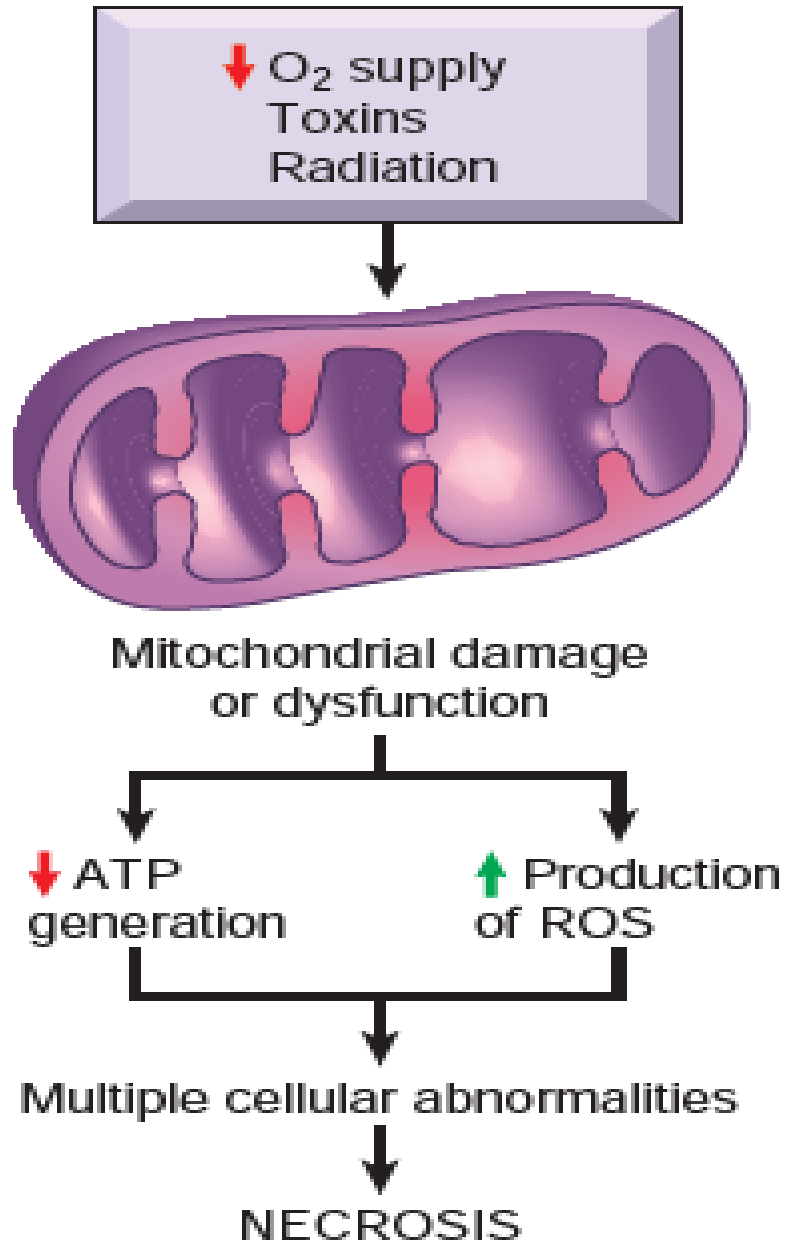
- 1. ATP depletion**
- 2. Mitochondrial Damage**
- 3. Loss of calcium homeostasis**
- 4. Defects in membrane permeability**
- 5. Free radical injury**

# Mitochondrial Damage





- Mitochondria are critical players in cell injury
- They supply life-sustaining energy by producing ATP  
**(Power house of cell)**



**Mitochondrial damage**



**Formation of a high-conductance channel in the mitochondrial membrane, called the mitochondrial permeability transition pore**



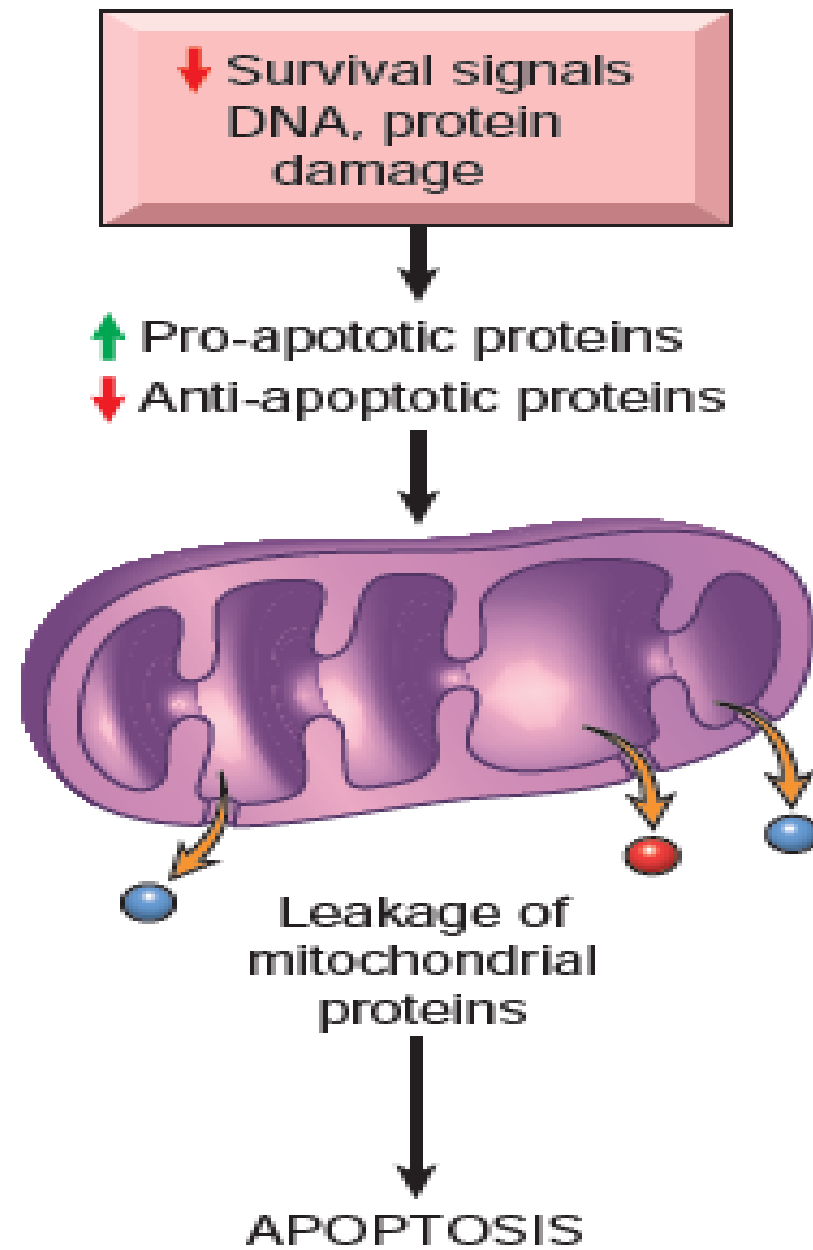
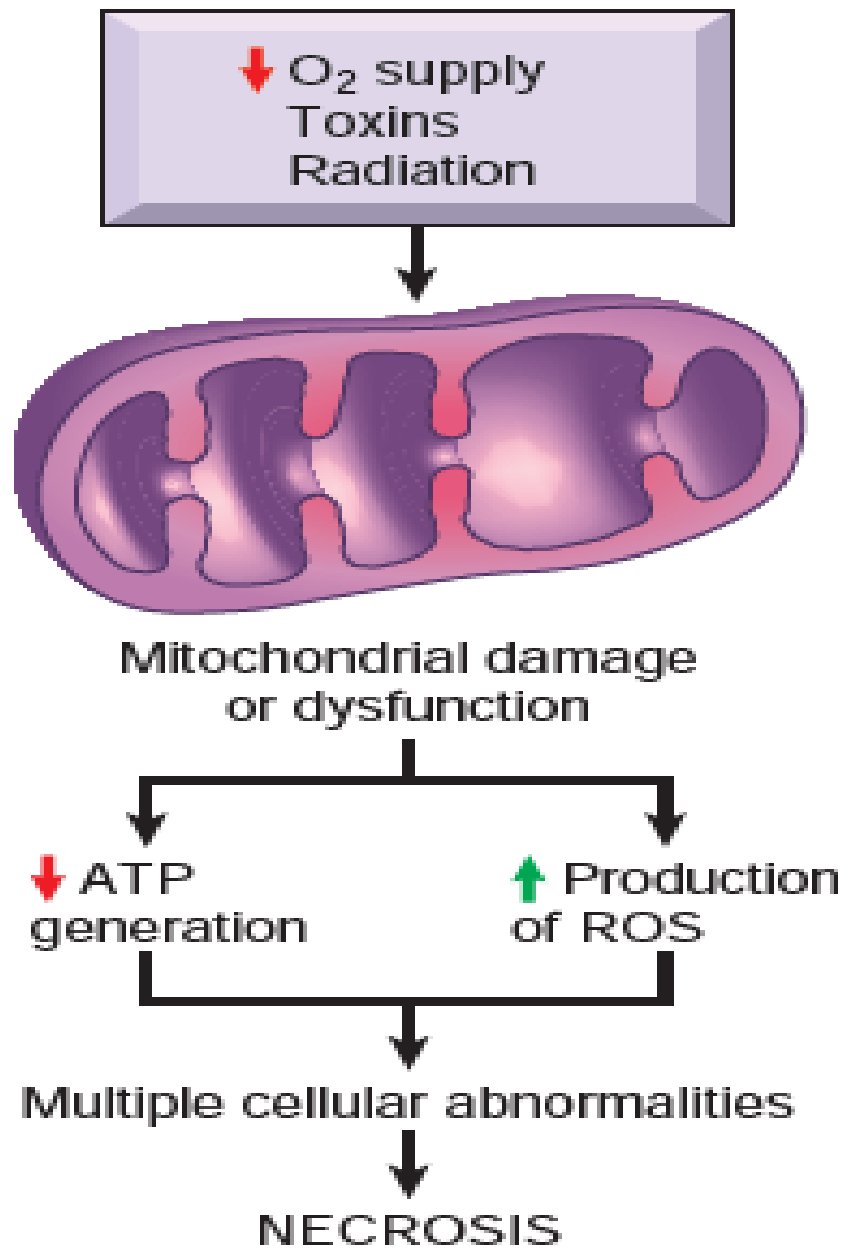
**Loss of mitochondrial membrane**



**Failure of NORMAL oxidative phosphorylation**



**Depletion of ATP**



**Mitochondrial damage**



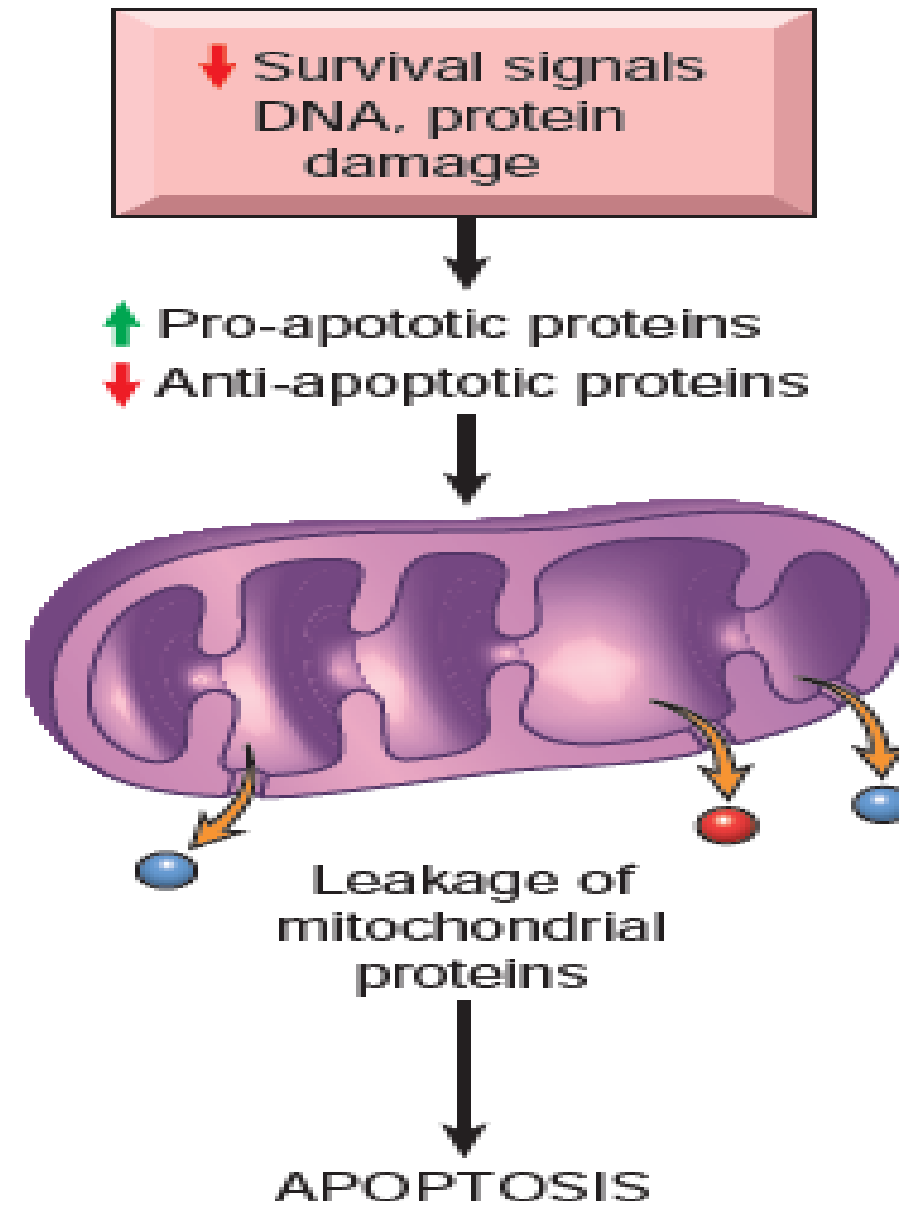
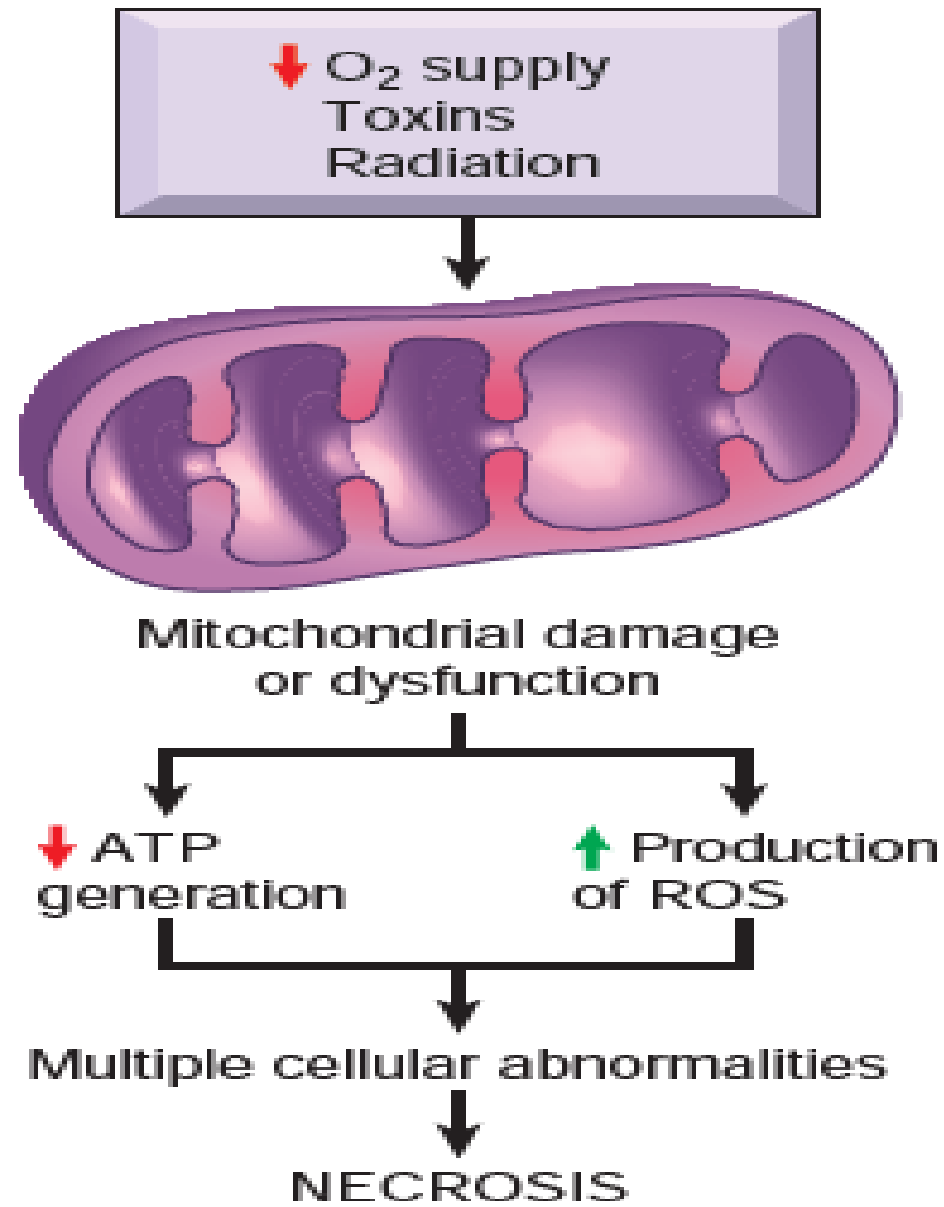
**Abnormal oxidative phosphorylation**



**Formation of reactive oxygen species (ROS)**



**Deleterious effects**



**The mitochondria sequester cytochrome c between their outer and inner membranes**



**Mitochondrial damage**



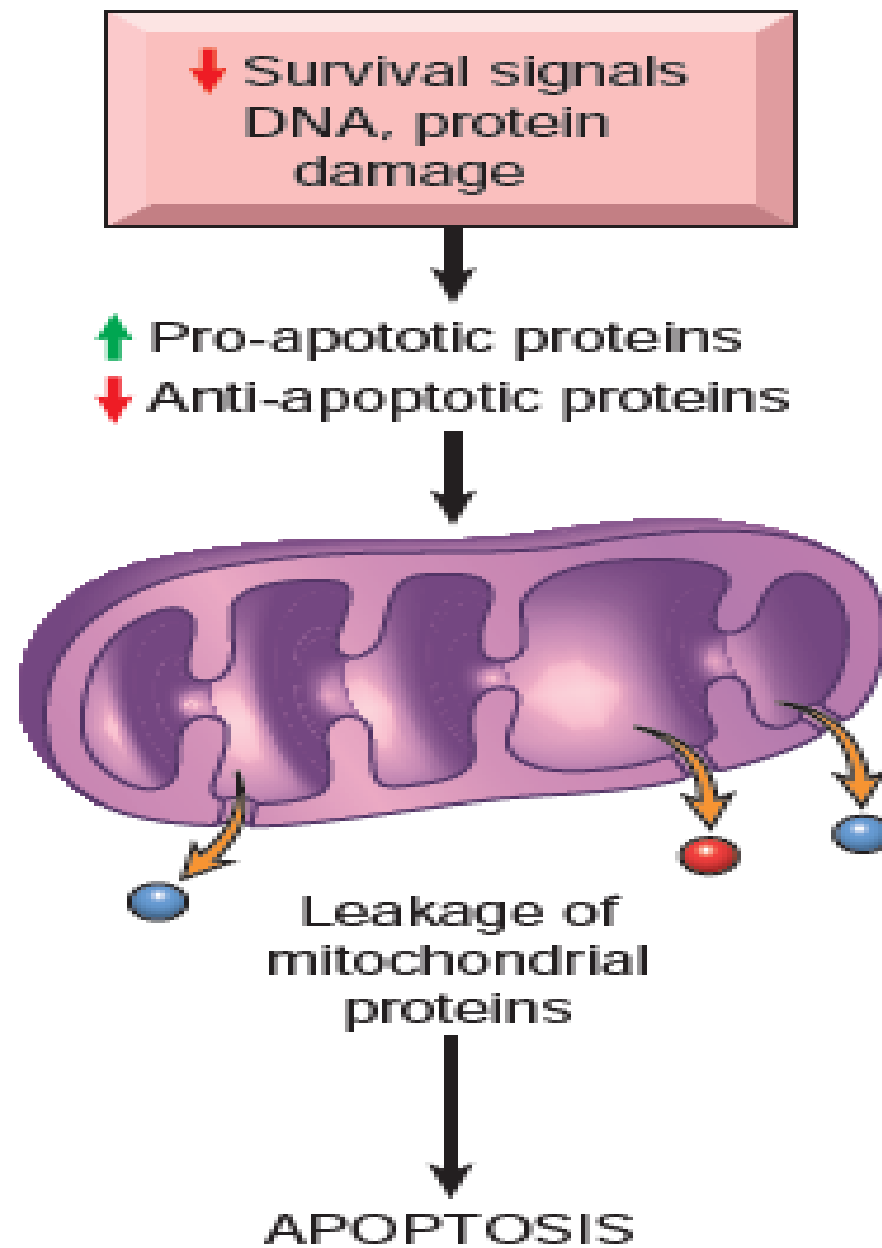
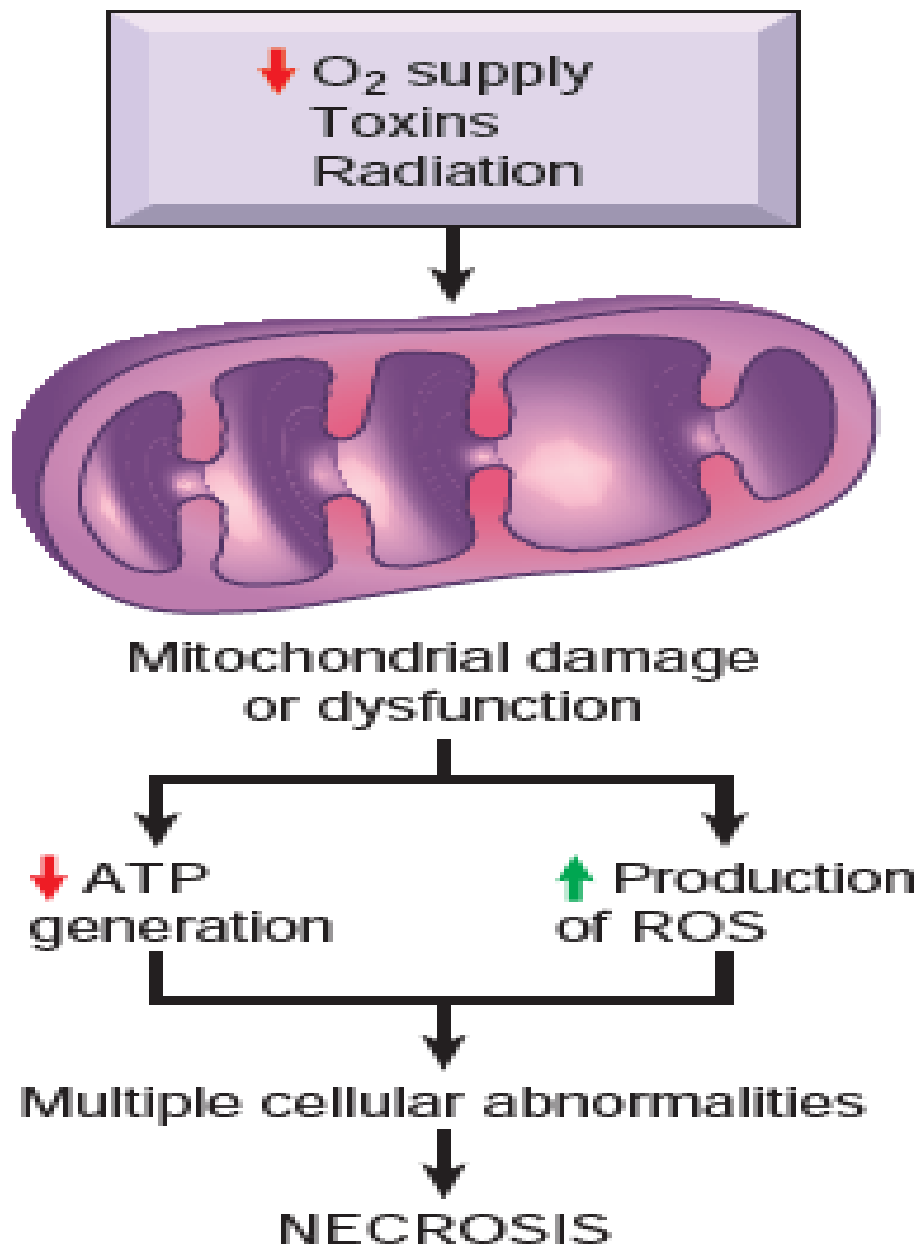
**Increased permeability of the outer mitochondrial membrane**



**leakage of cytochrome c into the cytosol**



**Apoptosis**





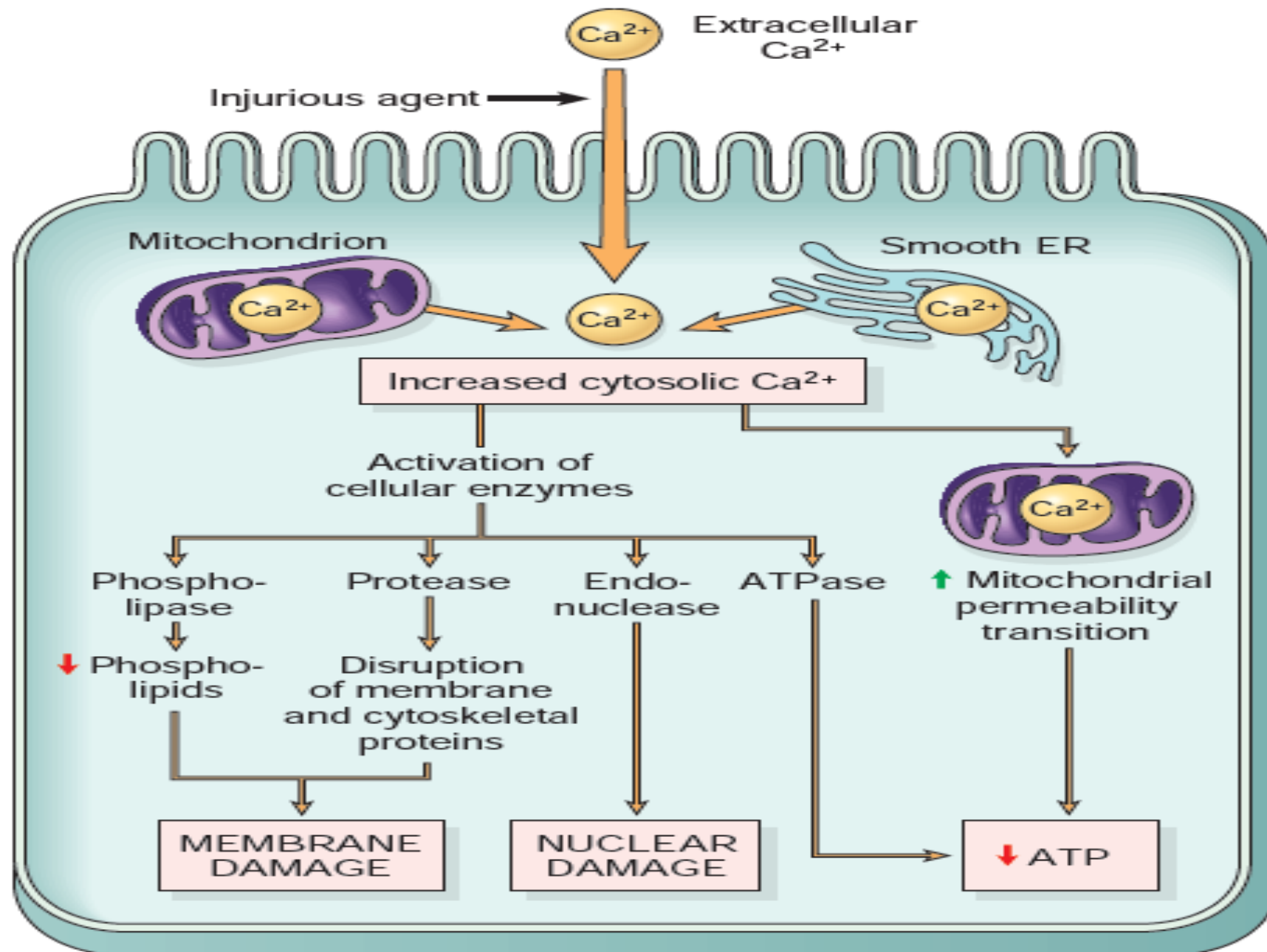
# **Mechanisms of Cell Injury**

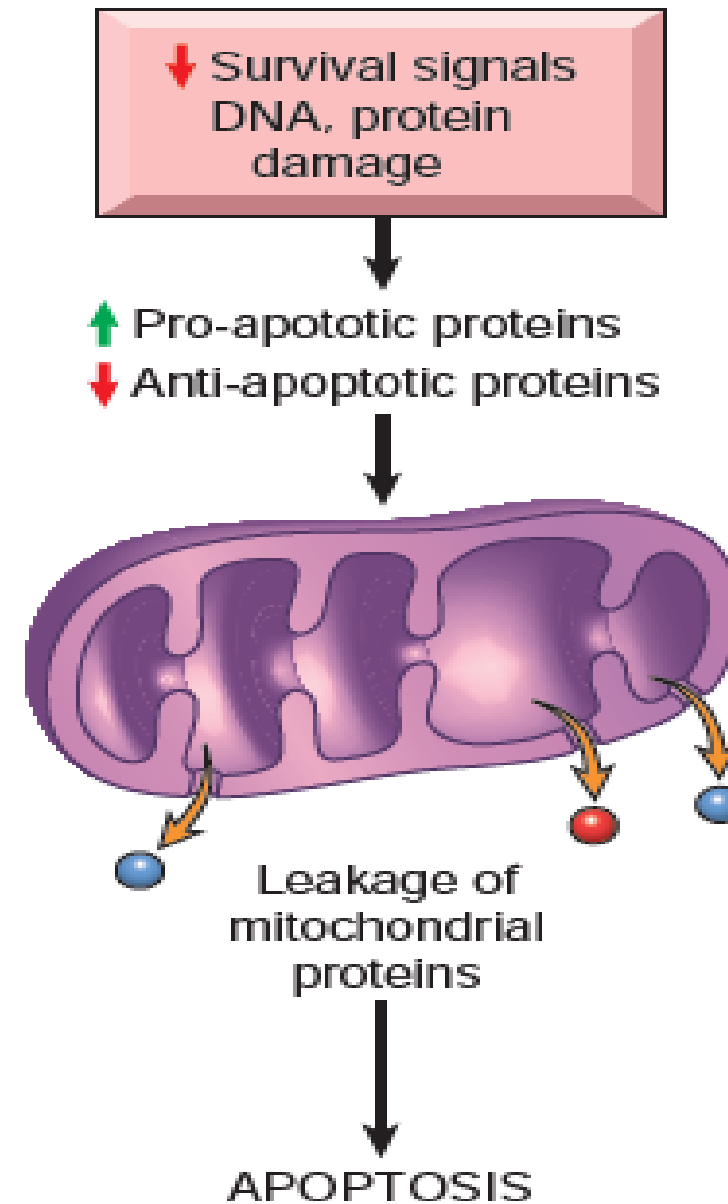
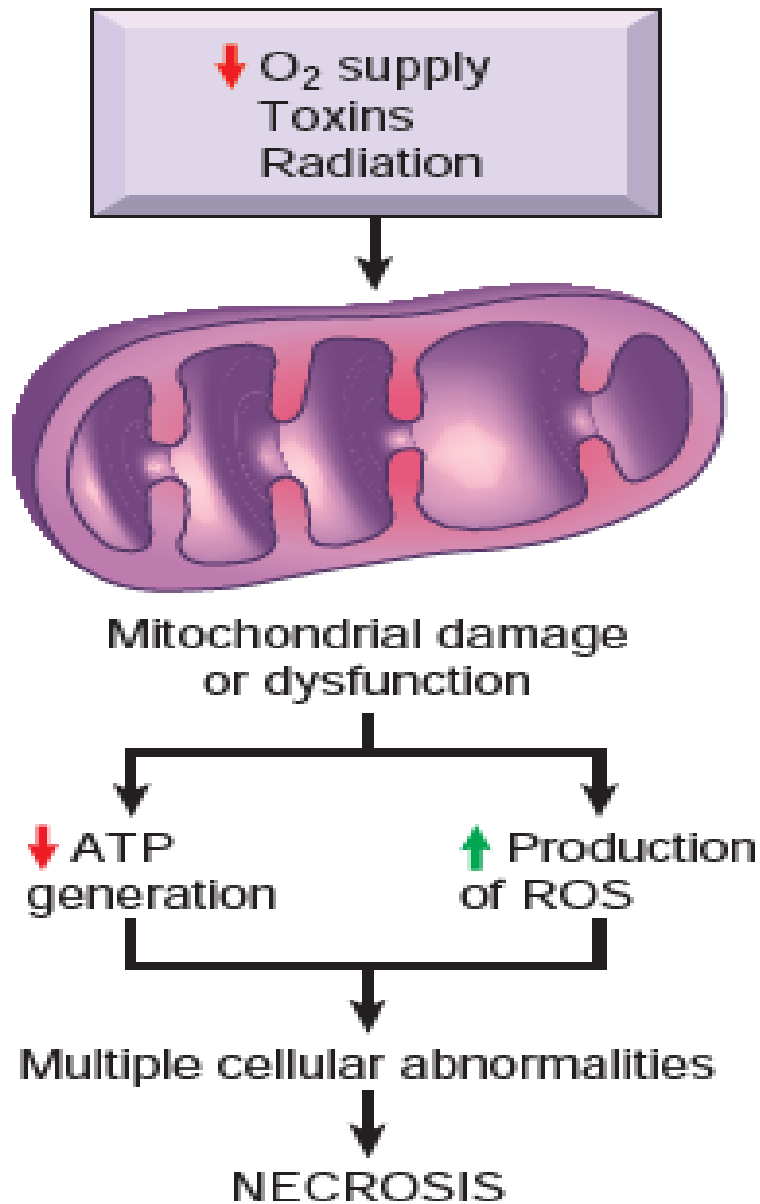
**5 mechanisms**→

- 1. ATP depletion**
- 2. Mitochondrial Damage**
- 3. Loss of calcium homeostasis**
- 4. Defects in membrane permeability**
- 5. Free radical injury**

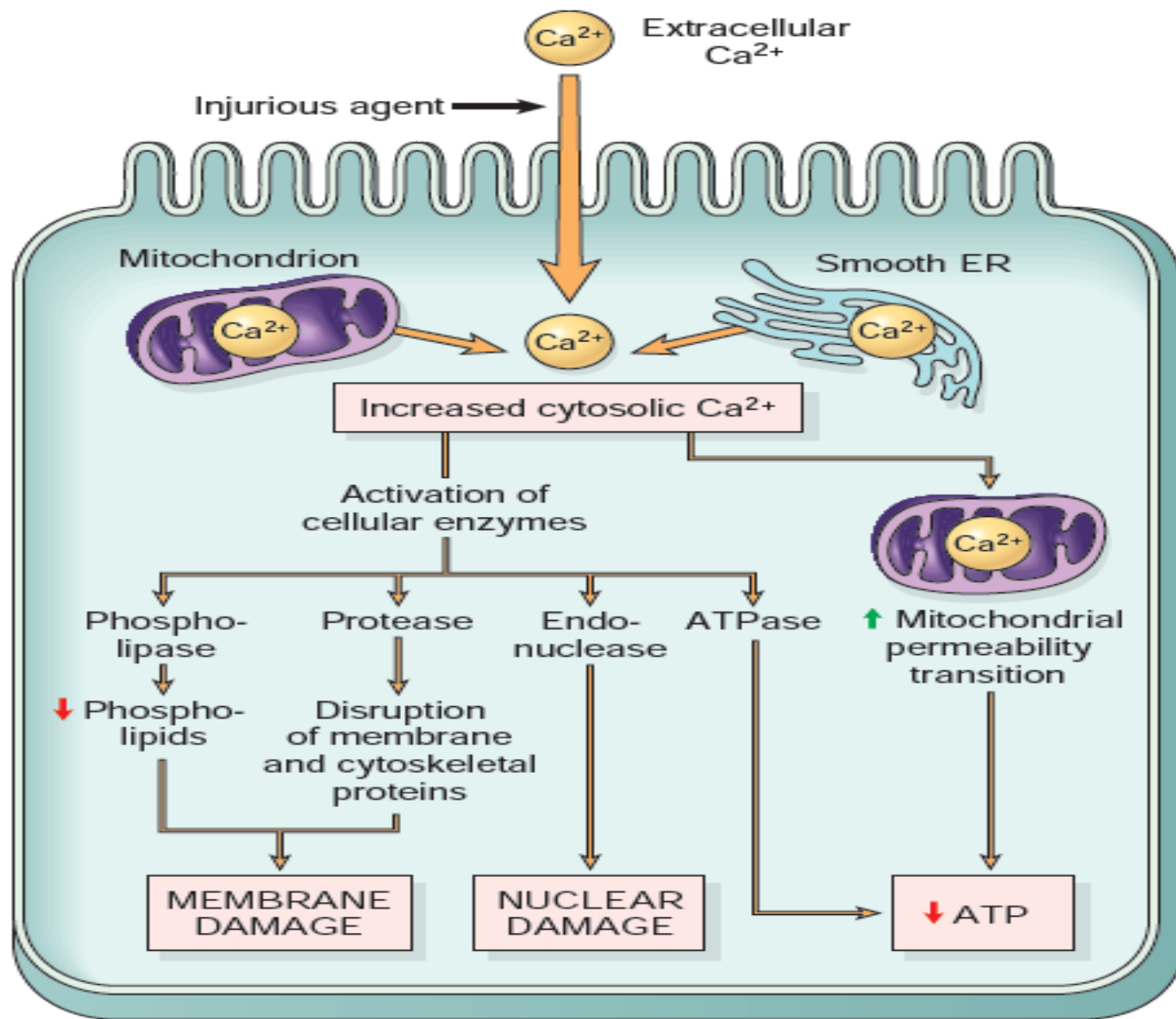
# Loss of calcium homeostasis







- **Intracellular free calcium** is very low compared with extracellular levels
- Most intracellular calcium is sequestered in **mitochondria and the ER.**



- Injury cause an increase in cytosolic  $\text{Ca}^{2+}$  because of →



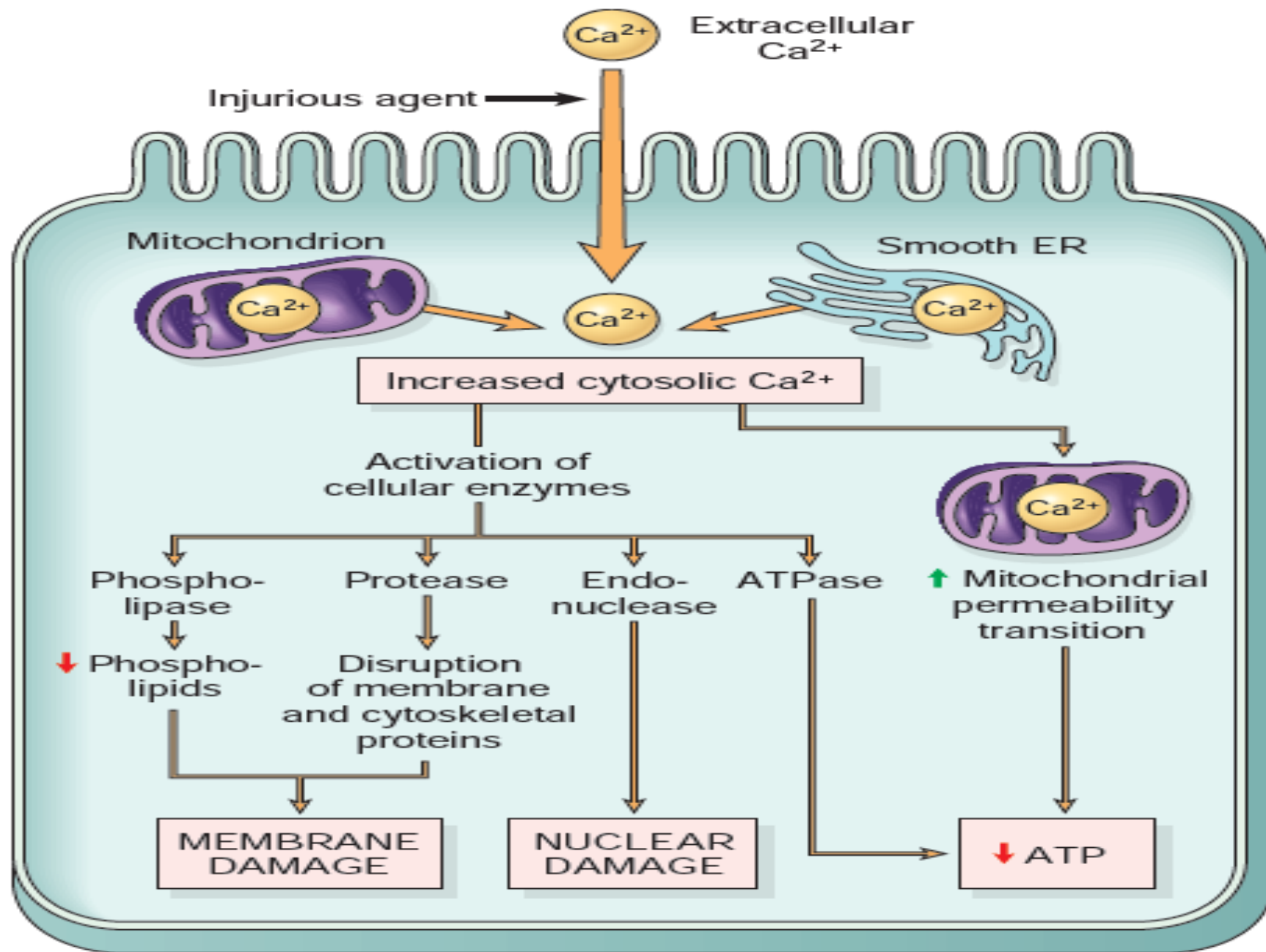
1. Increased influx across the plasma membrane
2. Release of  $\text{Ca}^{2+}$  from intracellular stores ie. mitochondria and the ER



Increased cytosolic  $\text{Ca}^{2+}$  activates a number of enzyme→



1. **Phospholipases** ( membrane damage),
2. **Proteases** ( breakdown both membrane and cytoskeletal proteins),
3. **Endonucleases** (DNA fragmentation)
4. **ATPases** (hastening ATP depletion)





**The accumulation of Ca<sup>2+</sup> in mitochondria**



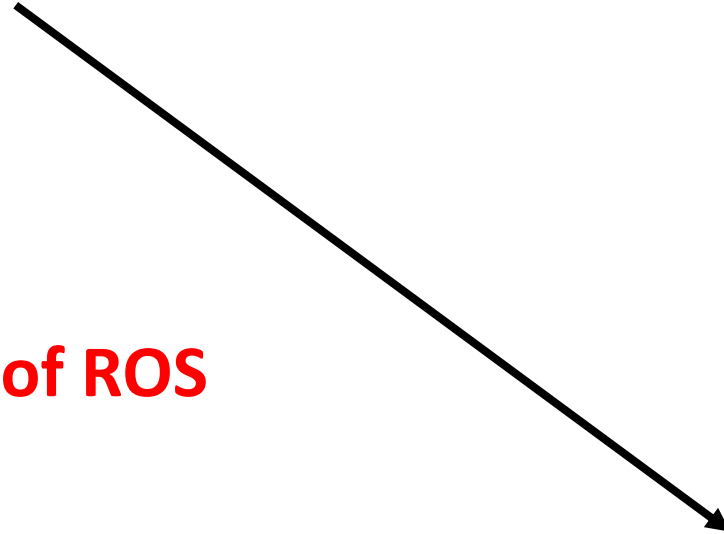
**Opening of the mitochondrial permeability transition pore**



**Failure of ATP generation**



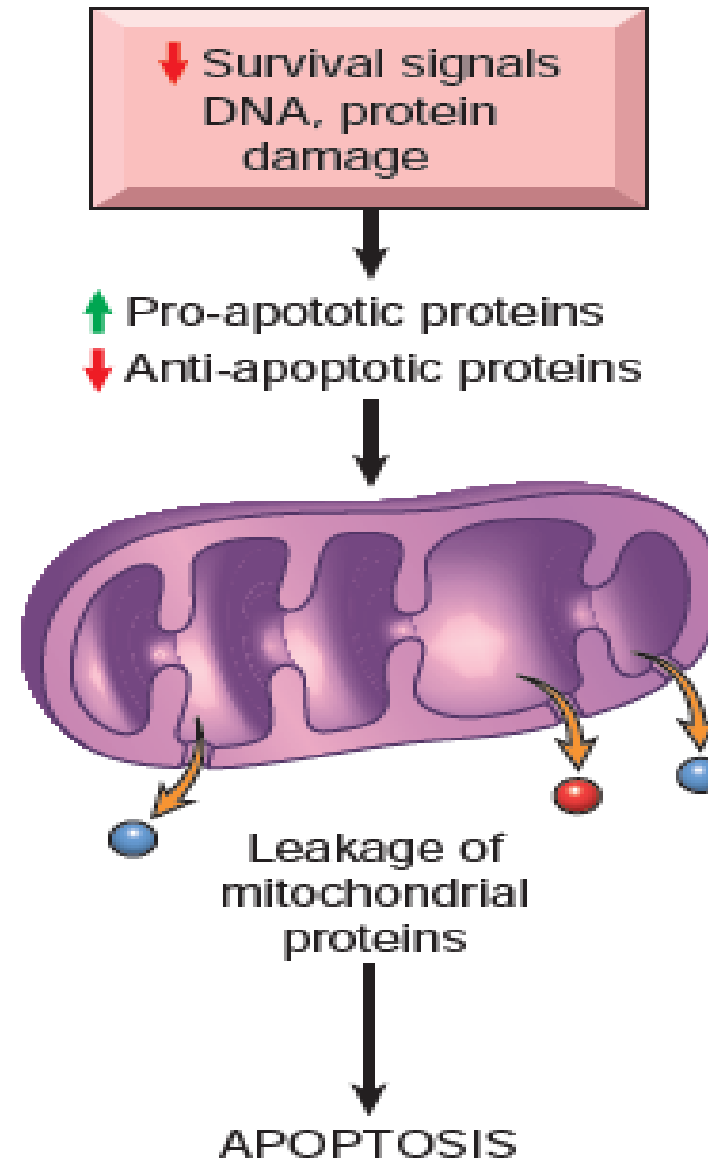
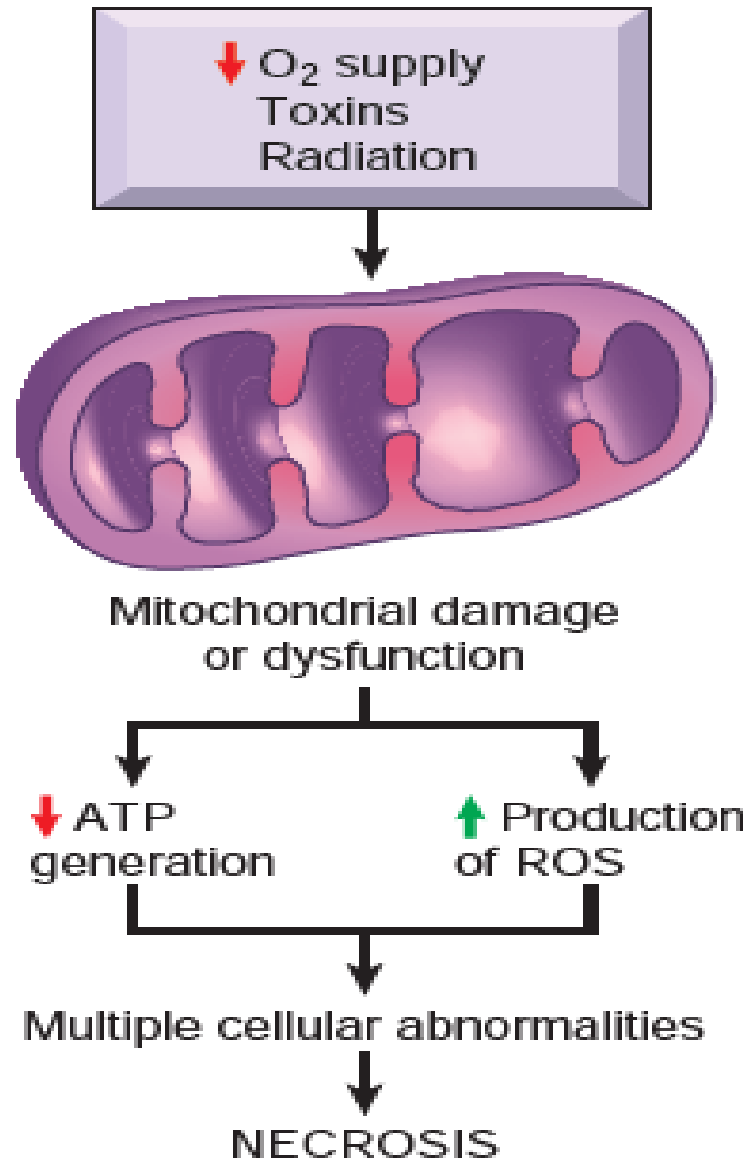
**Formation of ROS**



**Release of cytochrome c**



**Apoptosis**



# **Mechanisms of Cell Injury**

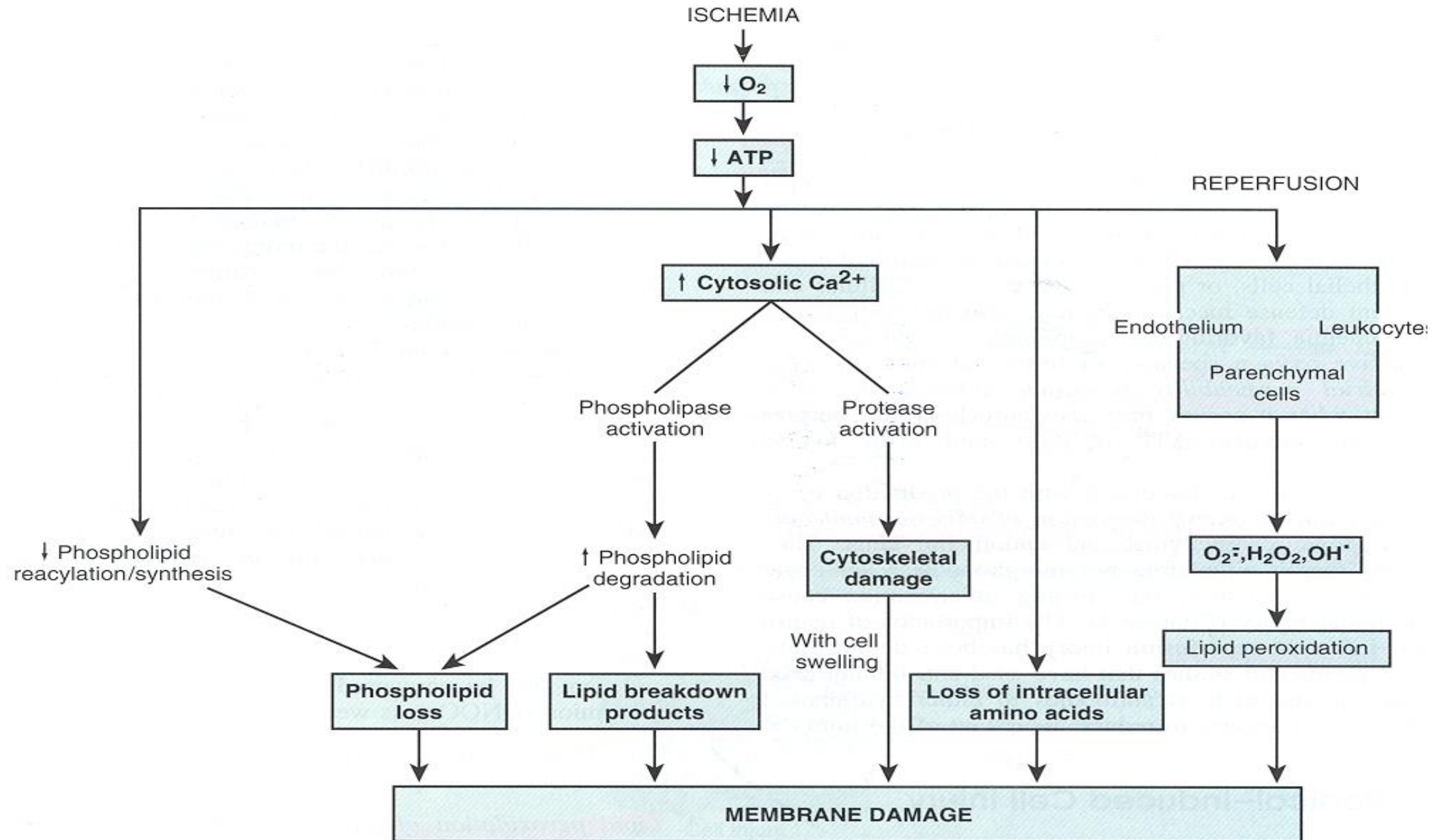
**5 mechanisms**→

- 1. ATP depletion**
- 2. Mitochondrial Damage**
- 3. Loss of calcium homeostasis**
- 4. Defects in membrane permeability**
- 5. Free radical injury**

# Defects in membrane permeability

Like us 





# **Consequences of Membrane Damage**

- 1. Mitochondrial membrane damage.**
- 2. Plasma membrane**
- 3. Lysosomal membrane damage**

# **Mitochondrial membrane damage**

**The accumulation of  $\text{Ca}^{2+}$  in mitochondria**



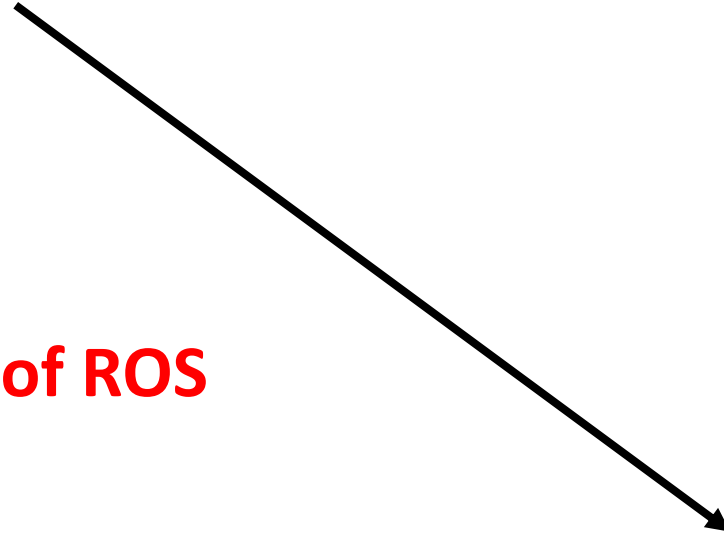
**Opening of the mitochondrial permeability transition pore**



**Failure of ATP generation**



**Formation of ROS**

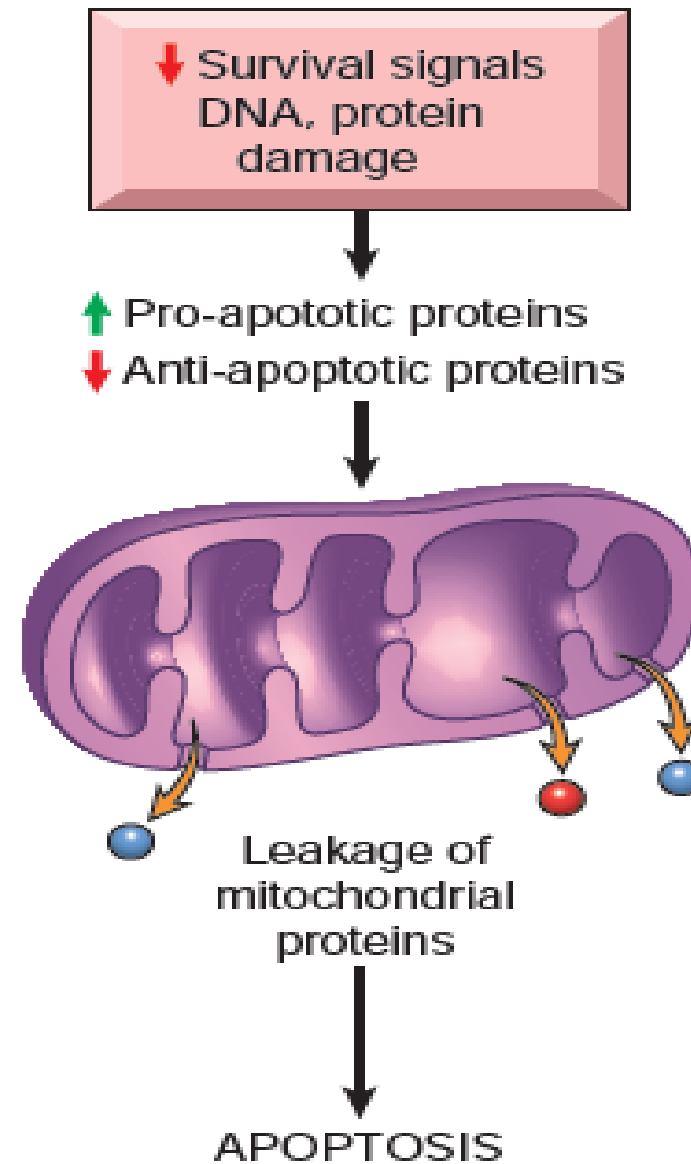
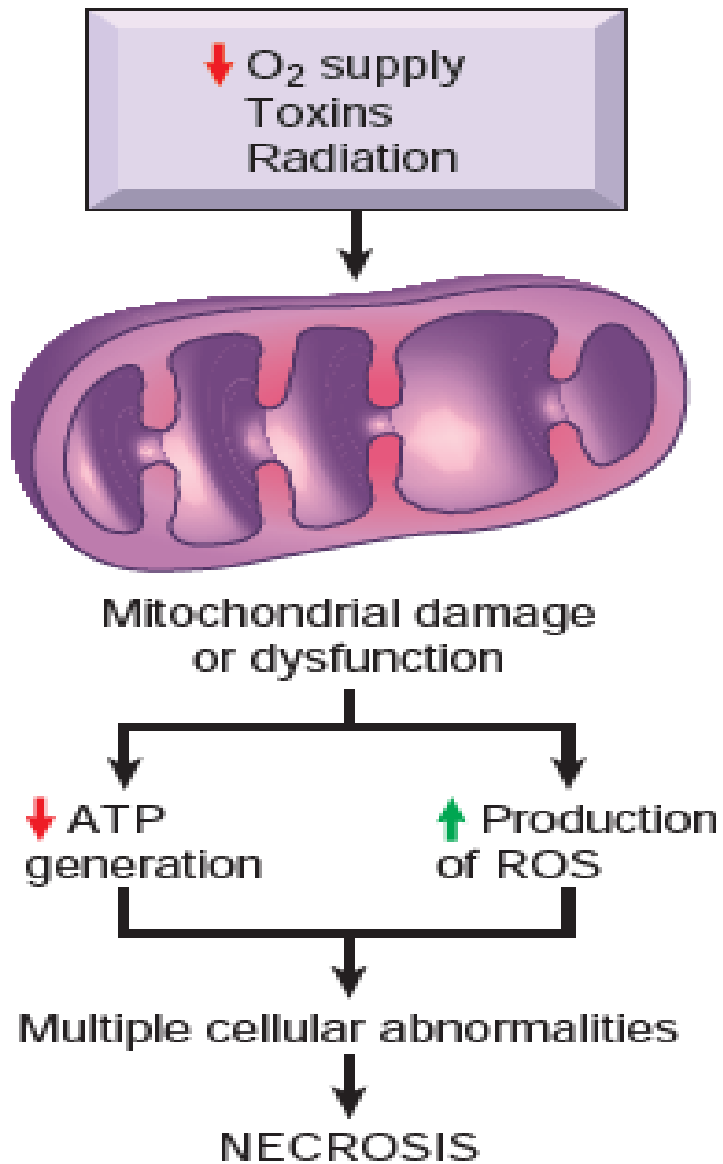


**Release of cytochrome c**



**Apoptosis**





# Plasma membrane damage

Loss of osmotic balance



Efflux of fluids and ions



Loss of cellular contents



Leak metabolites that are vital for the reconstitution of  
ATP

# **Lysosomal membrane damage**

**Lysosomes contain RNases, DNases, proteases, phosphatases, glucosidases, and cathepsins**



**Lysosomal membrane damage**



**leakage of their enzymes into the cytoplasm**



**enzymatic digestion of proteins, RNA, DNA, and glycogen**



**Necrosis**

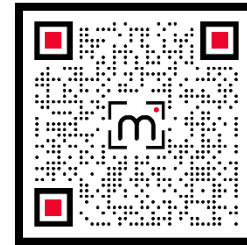
# **Mechanisms of Cell Injury**

**5 mechanisms**→

- 1. ATP depletion**
- 2. Mitochondrial Damage**
- 3. Loss of calcium homeostasis**
- 4. Defects in membrane permeability**
- 5. Free radical injury**

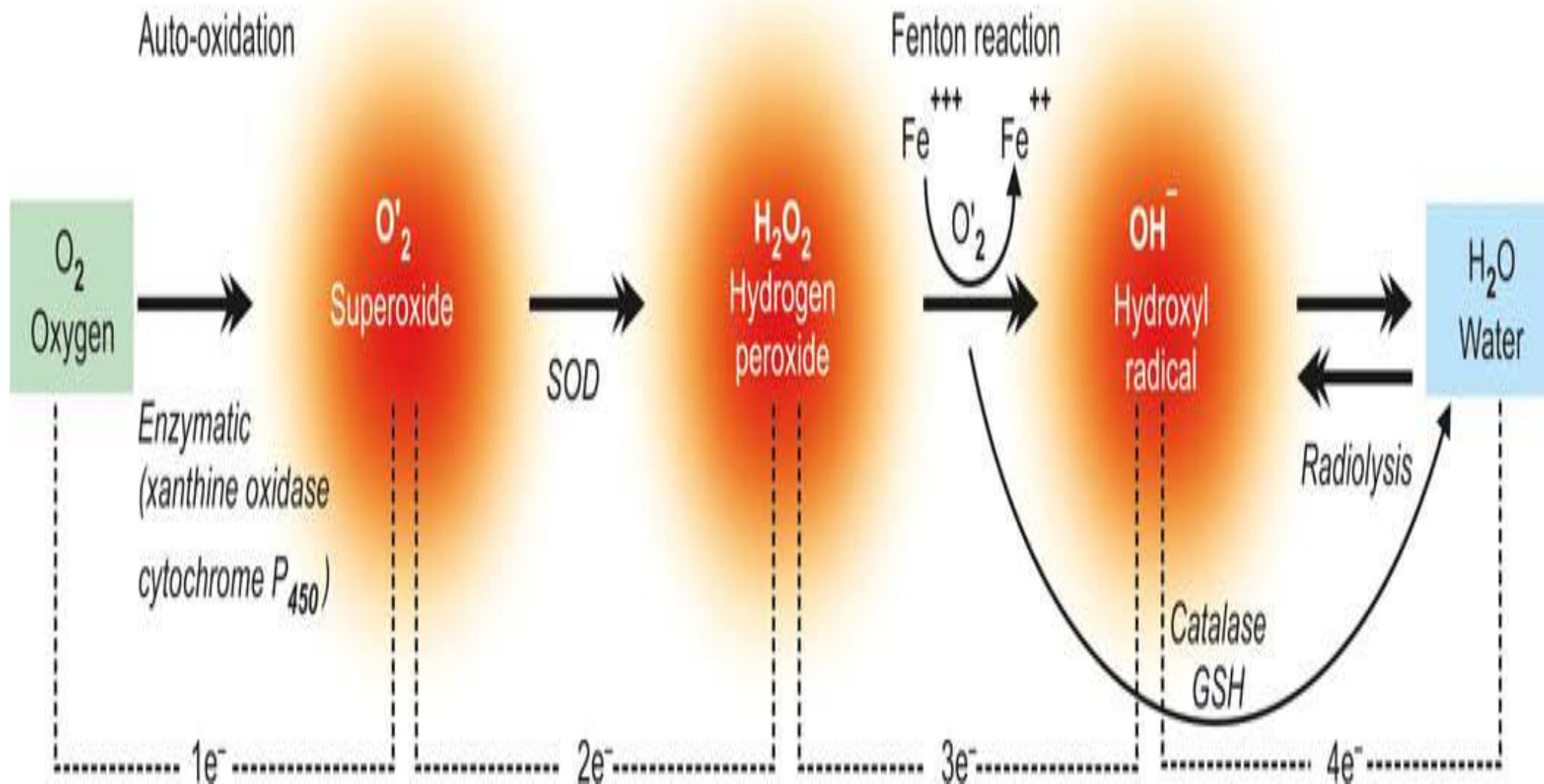
# FREE RADICAL INJURY

*Click or Scan QR code to join  
Telegram group discussion*



# FREE RADICAL INJURY

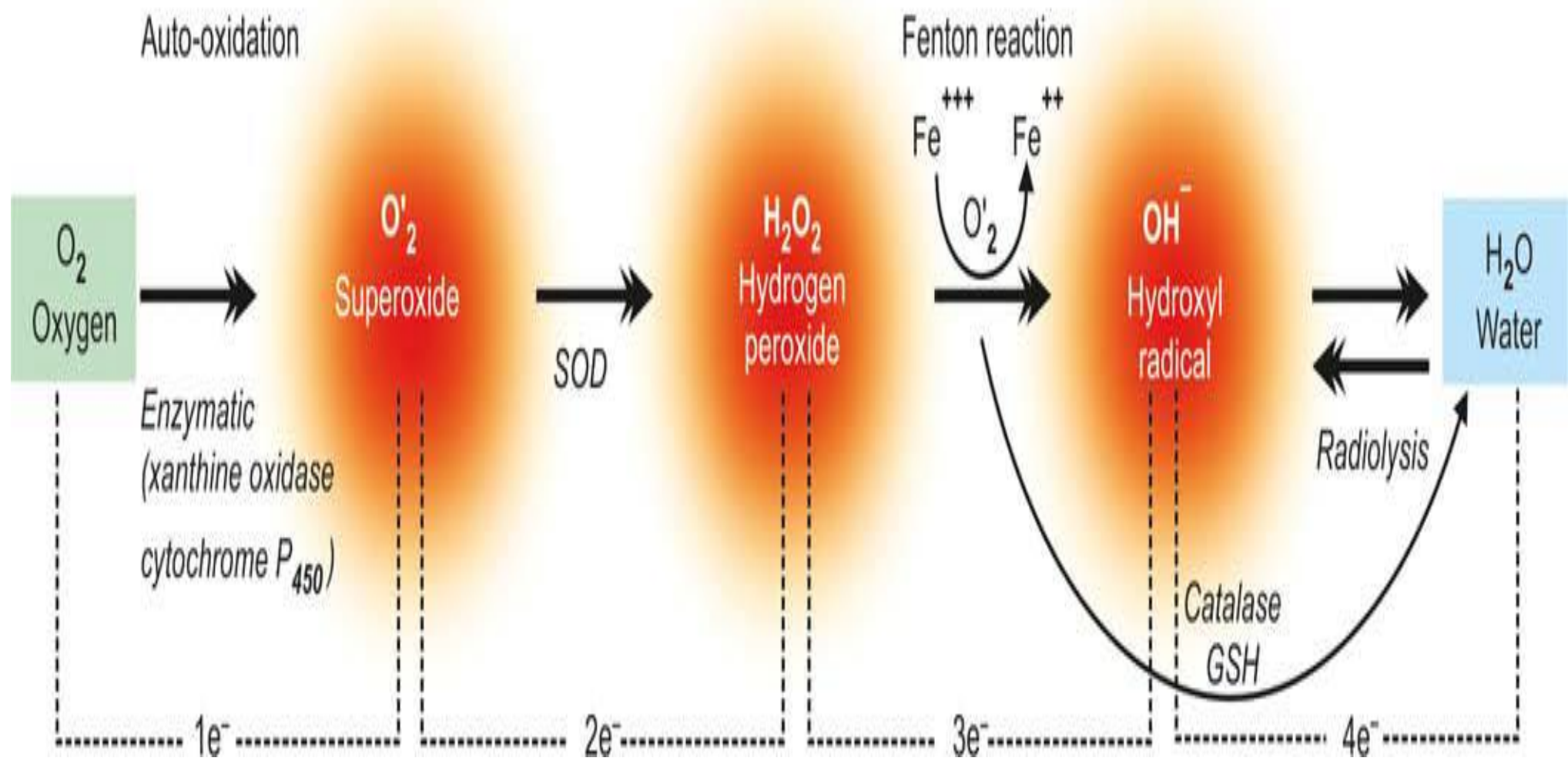
- Normally generation of ATP by oxidative process → oxygen ( $O_2$ ) combines with hydrogen atom (H), water ( $H_2O$ ) is formed
- This reaction of  $O_2$  to  $H_2O$  involves 'four electron donation' in four steps involving transfer of one electron at each step.



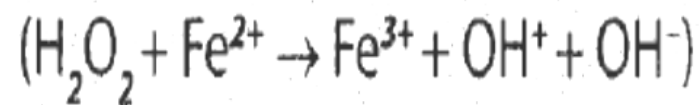
# Generation

- Free radicals are intermediate chemical species having a **single unpaired electron in its outer orbit.**
- Unpaired electrons are highly reactive and “attack” and modify inorganic or organic chemicals—proteins, lipids, carbohydrates, nucleic acids
- Generated within **mitochondrial inner membrane**
- Normally generation of ATP by oxidative process → oxygen ( $O_2$ ) combines with hydrogen atom (H), water ( $H_2O$ ) is formed

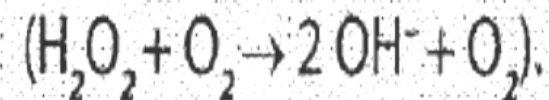




- **Fenton reaction** is involved in free radical generation when iron is converted from ferrous to ferric form <sup>(AIIMS 02)</sup>.



- **Haber-Weiss reaction** leads to generation of free radical ( $OH^\cdot$ ) during normal metabolic process



# Types

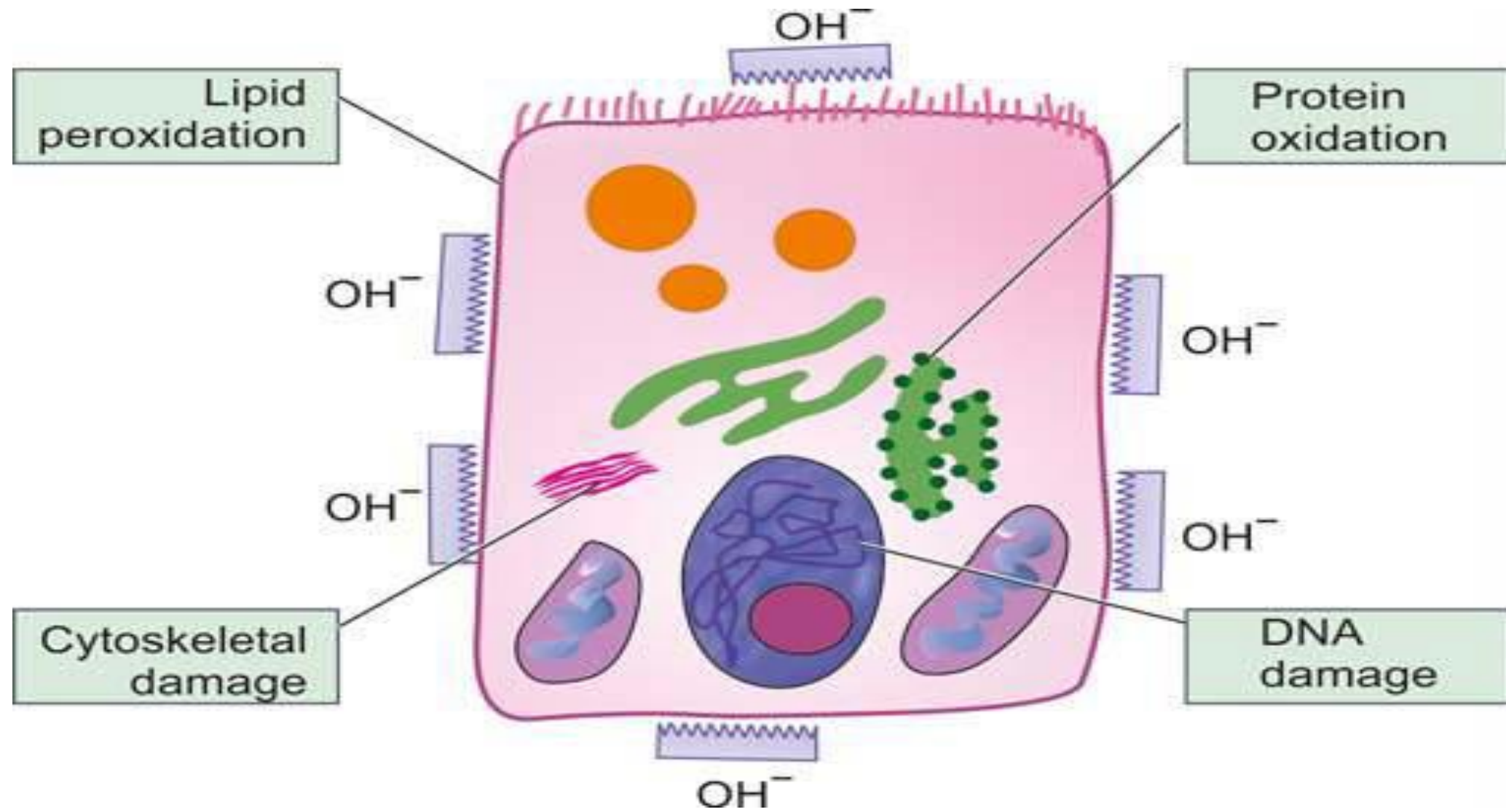
- 3 types depending upon the number of electrons transferred
1. Superoxide oxygen ( $\text{O}_2^-$ ): one electron
  2. Hydrogen peroxide ( $\text{H}_2\text{O}_2$ ): two electrons
  3. Hydroxyl radical ( $\text{OH}^\cdot$ ): three electrons

# Other free radicals

1. **Nitric oxide (NO):** NO is a chemical mediator formed by various body cells (endothelial cells, neurons, macrophages etc)
2. **Halide reagent (chlorine or chloride)**

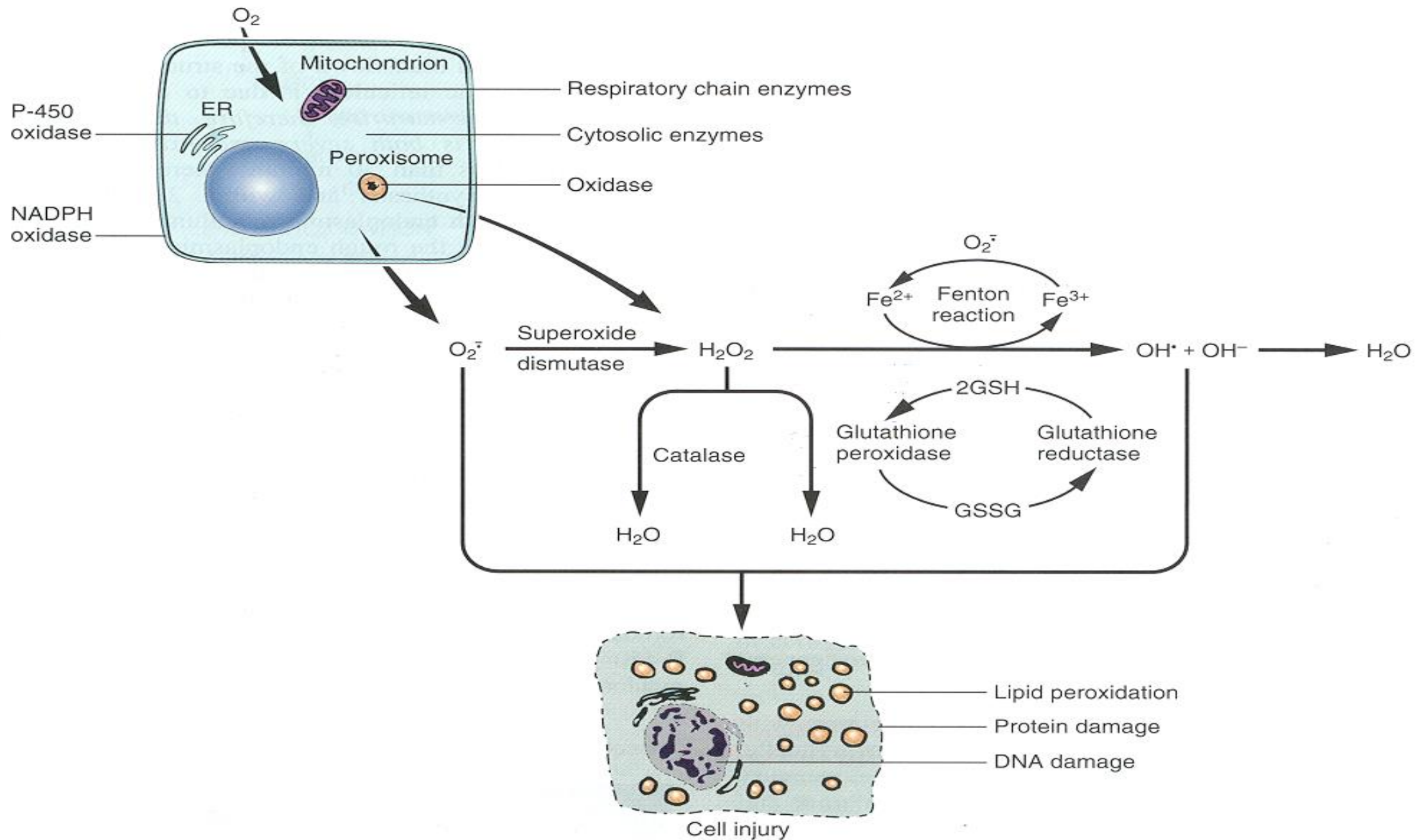
# What it causes

1. They react with, and **damage proteins, lipids, carbohydrates, nucleic acids**
2. Lipid peroxidation in cell membranes,
3. Oxidation of amino acids and proteins resulting in fragmentation
4. Protein-protein cross linkages.



# REMOVAL

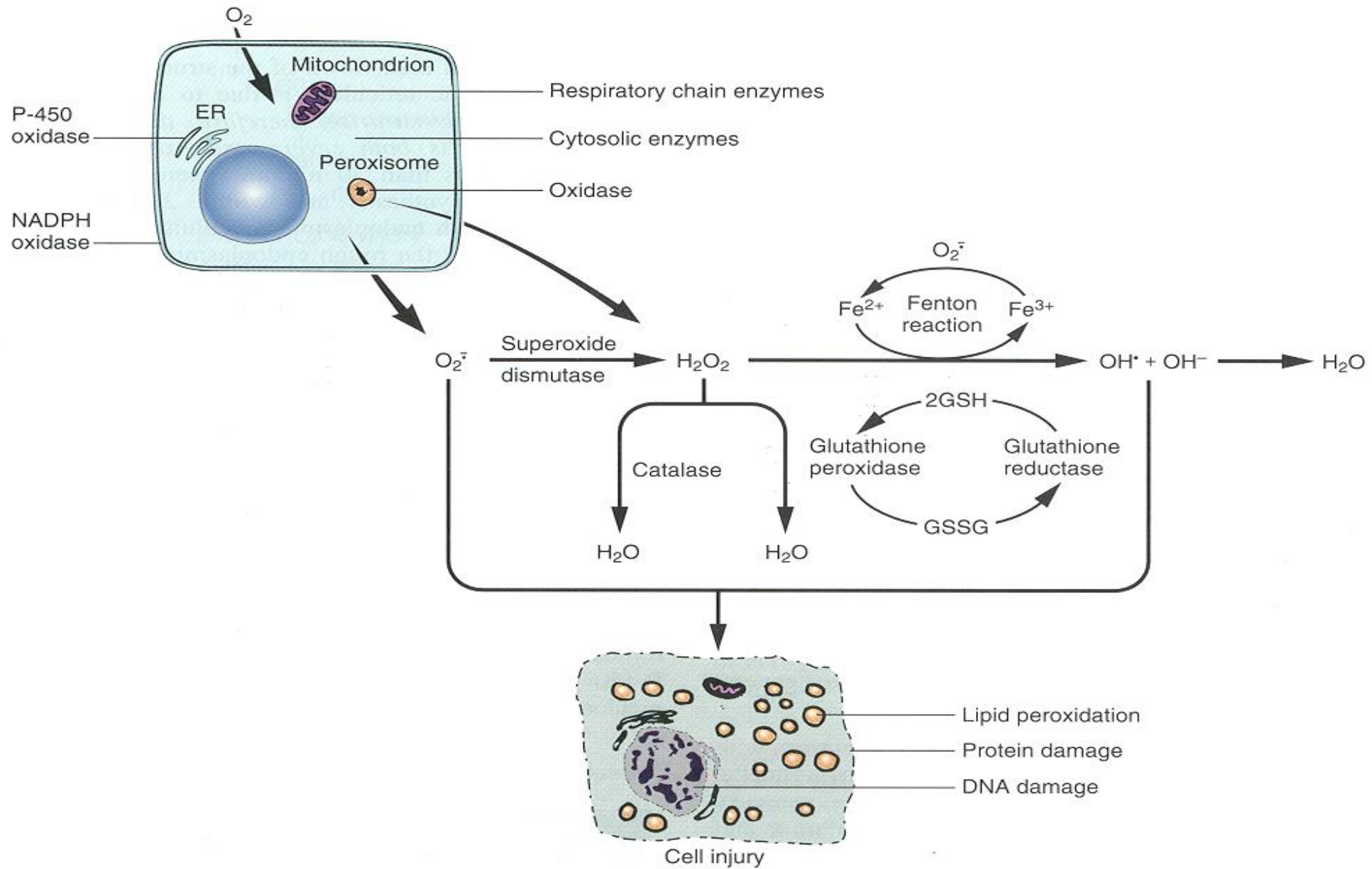
1. Superoxide dismutase
2. Glutathione peroxidase
3. Catalase
4. Vitamin E, vitamin C
5. Transferrin, ferritin and ceruloplasmin  
(Iron and copper catalyze free radical formation )





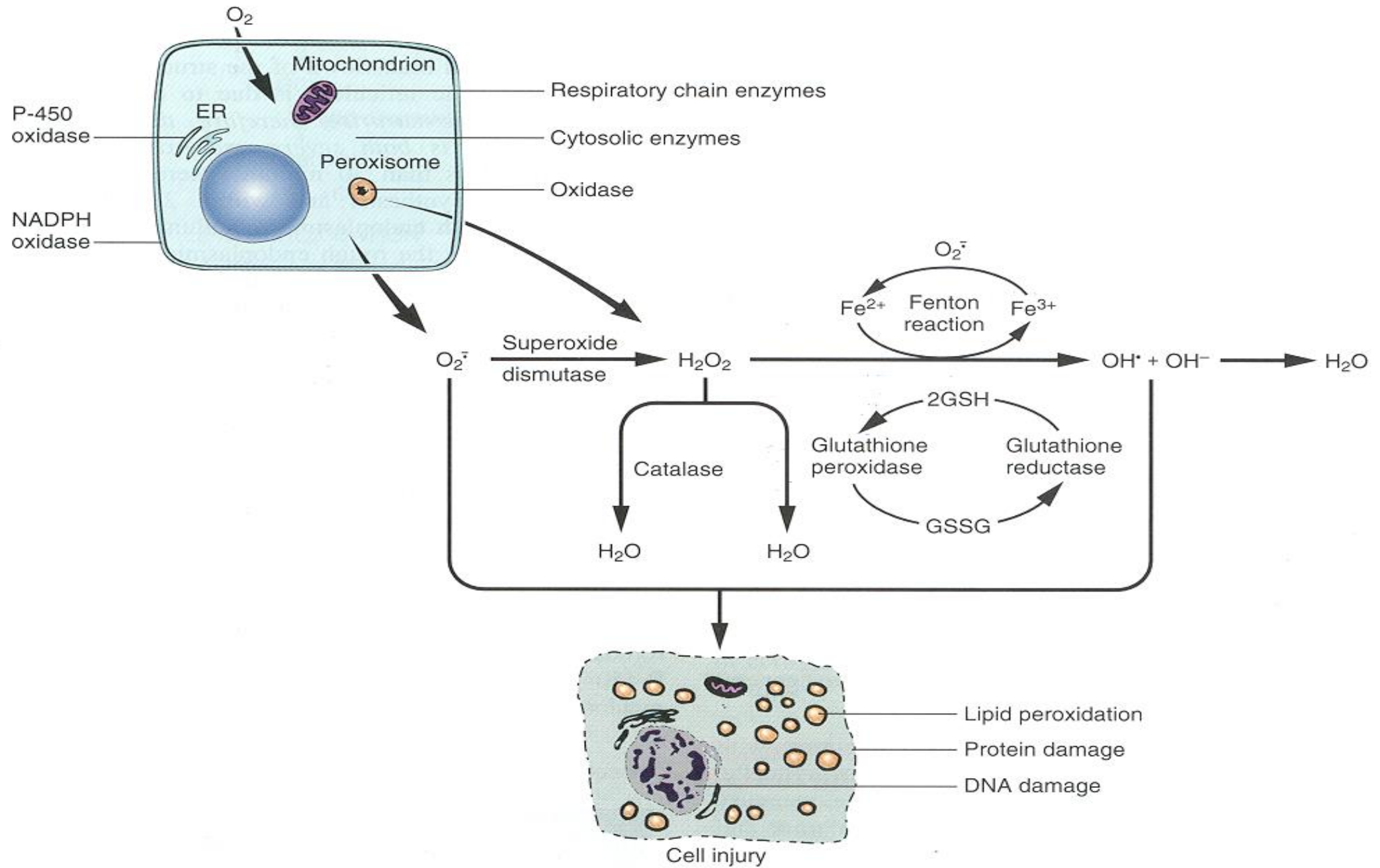
# Superoxide dismutase (SOD)

- Superoxide dismutase (SOD) is present in **mitochondria (manganese-SOD) and in cytosol (copper-zinc- SOD)**.
- It converts superoxide to  $\text{H}_2\text{O}_2$
- $2\text{O}^- + 2\text{H} \rightarrow 2\text{H}_2\text{O}_2 + \text{O}_2$



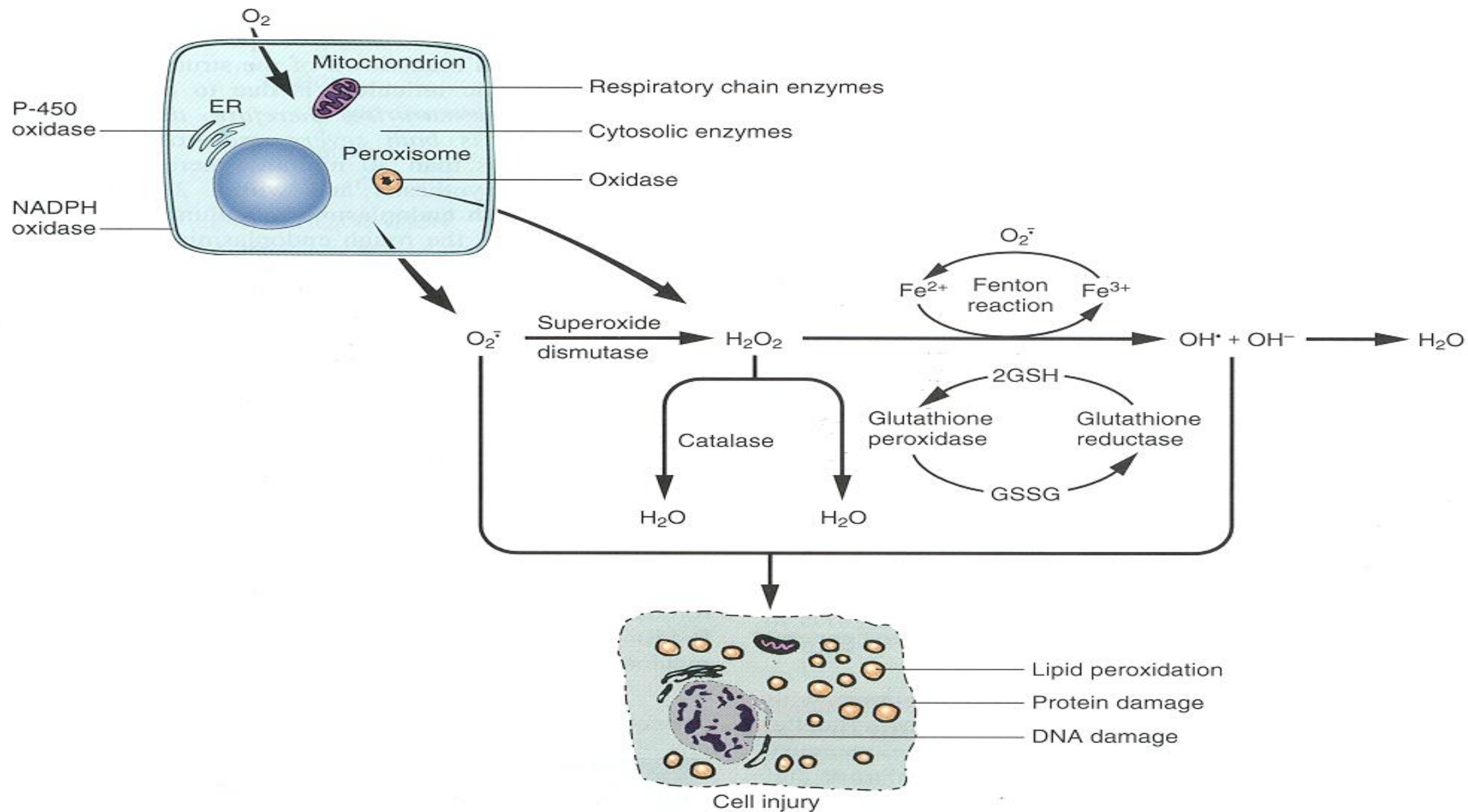
# Glutathione peroxidase

- Glutathione peroxidase is present in **mitochondria and cytosol**
- Intracellular ratio of oxidized glutathione (GSSG) to reduced glutathione (GSH) is a reflection of the oxidative state of the cell.



# Catalase

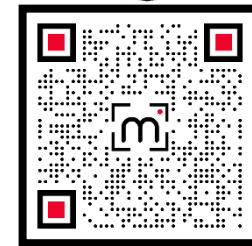
- Catalase is present in **peroxisomes**
- $2\text{H}_2\text{O}_2 \rightarrow \text{O}_2 + 2\text{H}_2\text{O}$

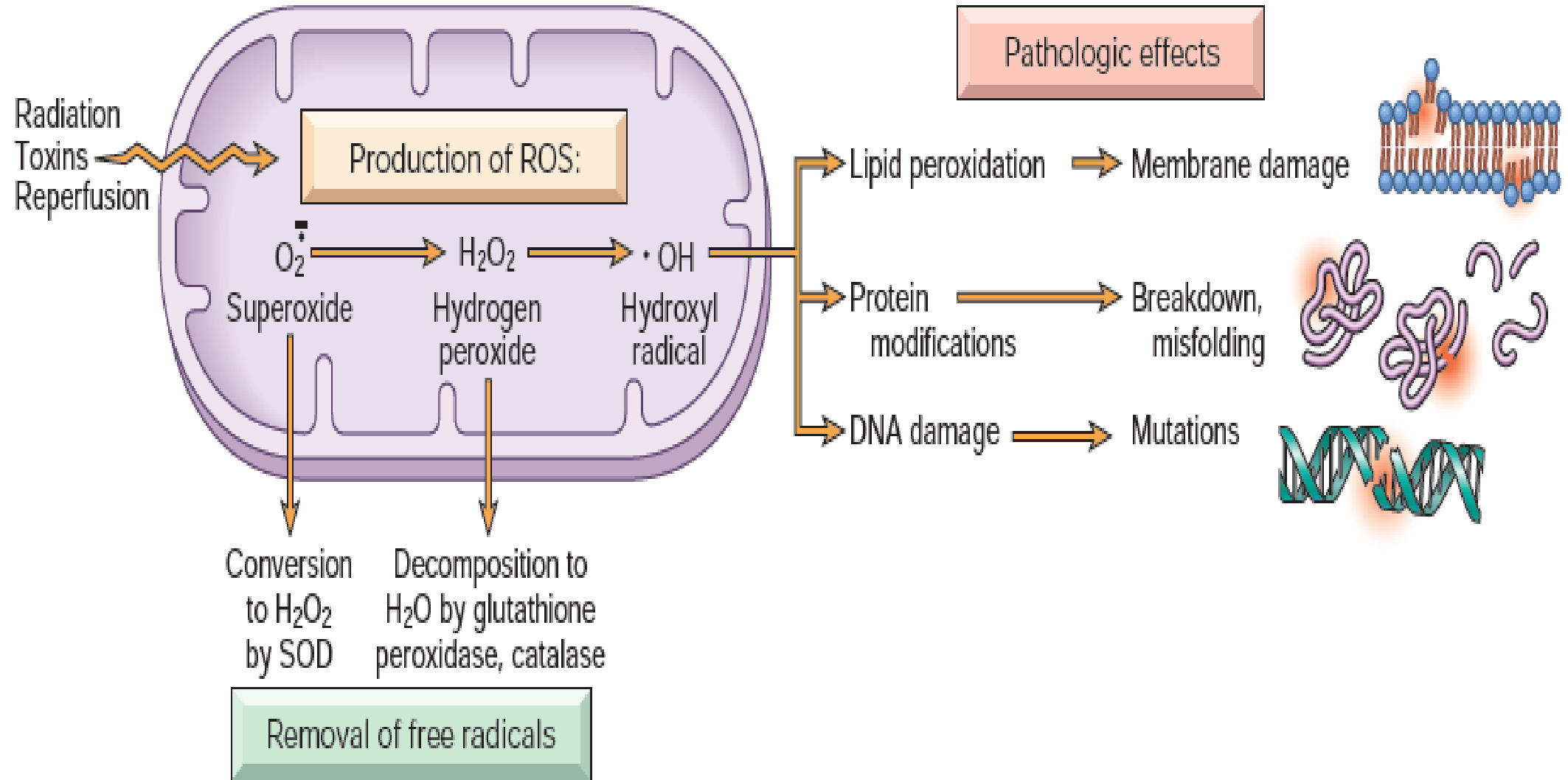


# REMEMBER

- $\text{H}_2\text{O}_2$  is produced as well as degraded in: peroxisomes, mitochondria and cytosol.

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Telegram group discussion*







# **Mechanisms of Cell Injury**

**5 mechanisms**→

- 1. ATP depletion**
- 2. Mitochondrial Damage**
- 3. Loss of calcium homeostasis**
- 4. Defects in membrane permeability**
- 5. Free radical injury**

# POLLS 2

*Scan or Click to watch  
Cell Adaptation & Injury*



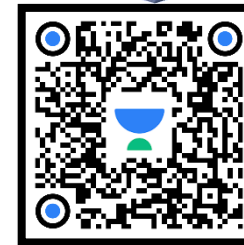
*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*



**Deadliest free radical is -**

- a) Hydrogen peroxide ( $\text{H}_2\text{O}_2$ )
- b) Superoxide anion ( $\text{O}_2^-$ )
- c) Hydroxyl ion ( $\text{OH}$ )
- d) Peroxynitrite ( $\text{OONO}^-$ )

**c**

**The Fenton reaction leads to free radical generation when -**

- a) Radiant energy is absorbed by water
- b) Hydrogen peroxide is formed by myeloperoxidase
- c) Ferrous ions are converted to ferric ions
- d) Nitric oxide is converted to peroxynitrite anion

**C**

**Which of the following is not a free radical scavenger-**

- a) Glutathione peroxidase
- b) Superoxide dismutase
- c) Catalase
- d) Xanthine oxidase

# D

follow us





**Enzyme that protects the brain from free radical injury is -**

- a) Myeloperoxidase
- b) Superoxide dismutase
- c) MAO
- d) Hydroxylase

**B**

**Organelle where  $\text{H}_2\text{O}_2$  is produced and destroyed is-**

- a) Peroxisome
- b) Lysosome
- c) Golgi body
- d) Ribosome

**A**

# Headings

- Introduction
- Definition
- Types of cell injury
- Etiology
- Mechanisms → 5
- Morphology

# Morphology of Cell Injury



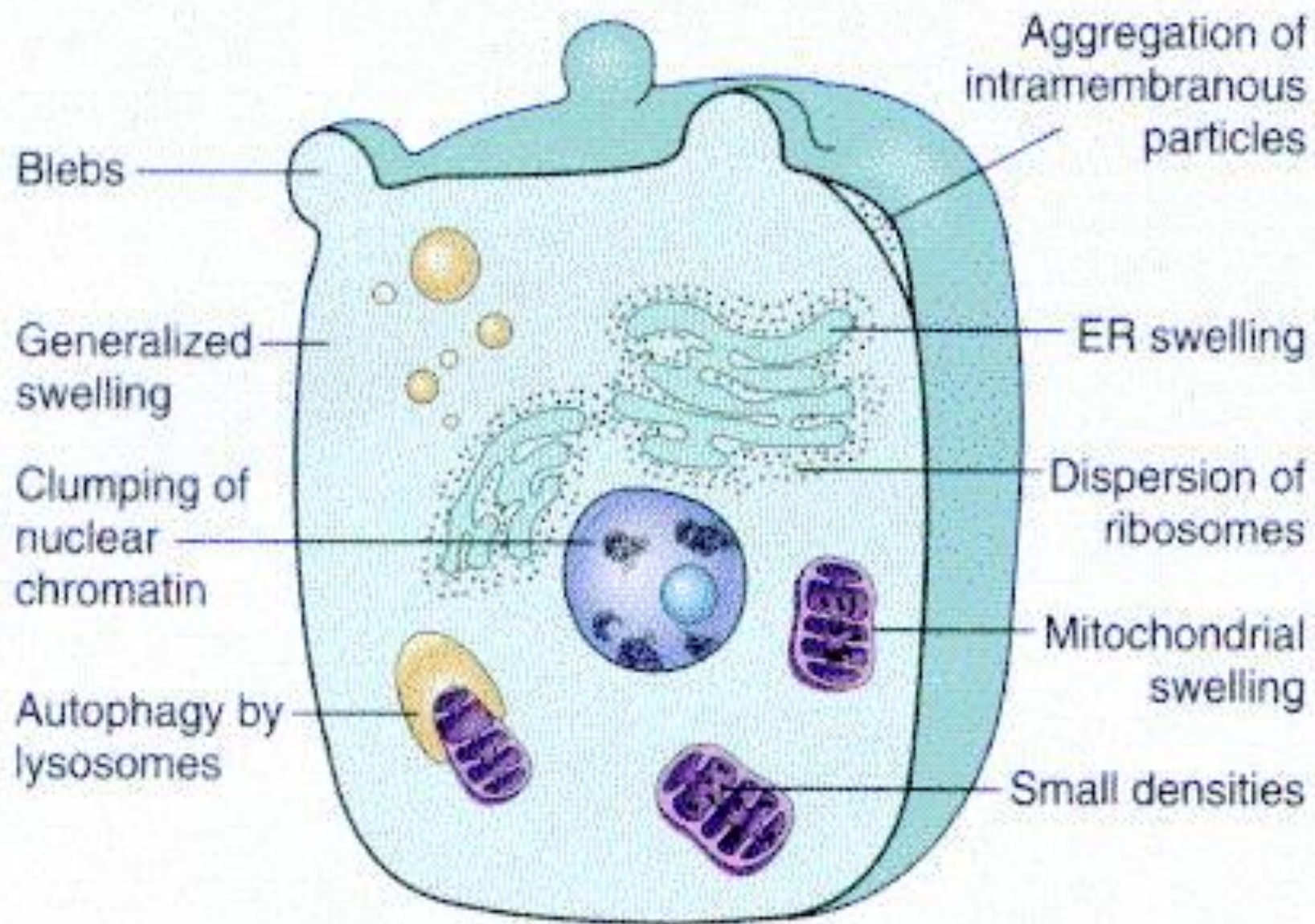
# **Reversible cell injury**

- Functional and morphologic changes are reversible if the damaging stimulus is removed.

# Irreversible injury and cell death

- With continuing damage → point of no return → injury becomes irreversible.
- Cells undergo morphologic changes recognisable as cell death.
- Cell death is of 2 types → **necrosis and apoptosis**





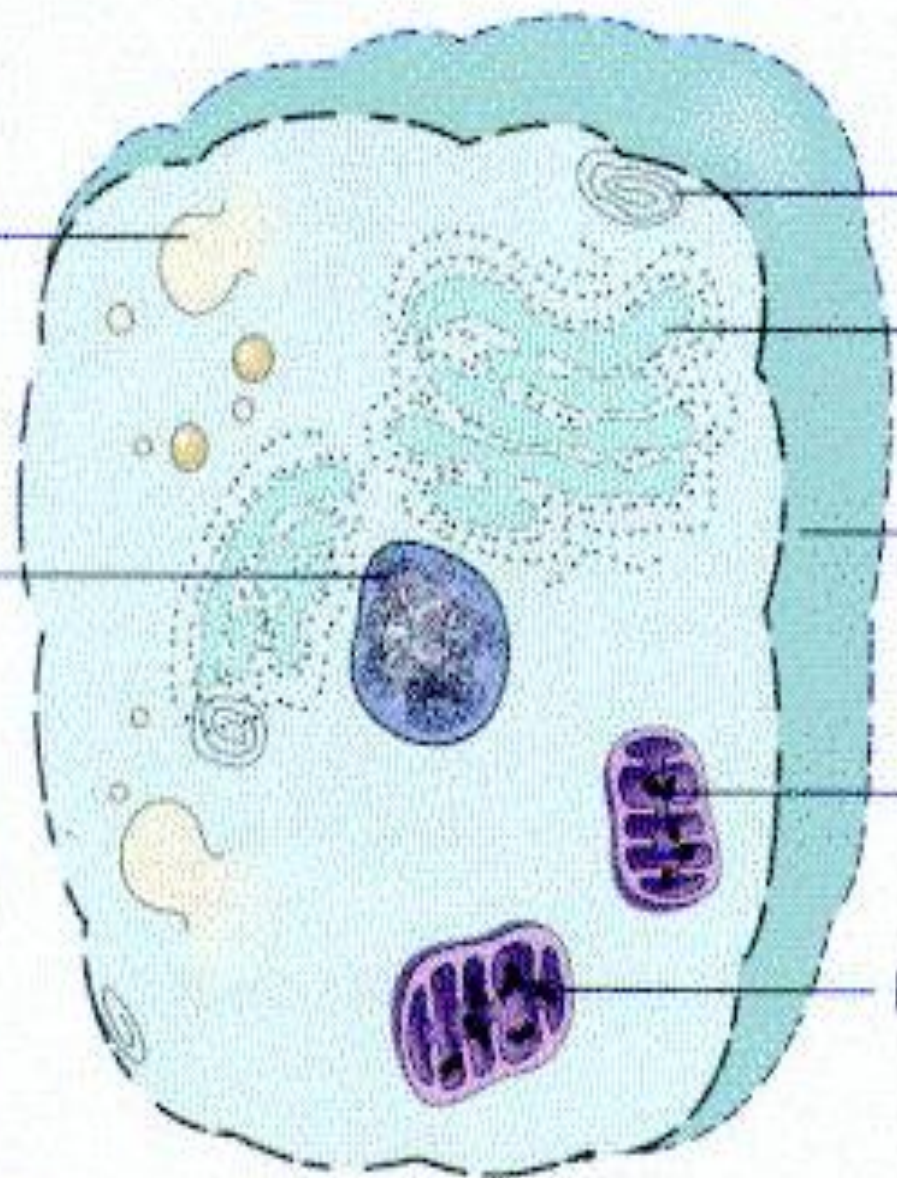
B. Reversible injury

Rupture of  
lysosomes  
and  
autolysis

Nucleus:  
• pyknosis  
or

• karyolysis  
or

• karyorrhexis



Myelin  
figures

Lysis of ER

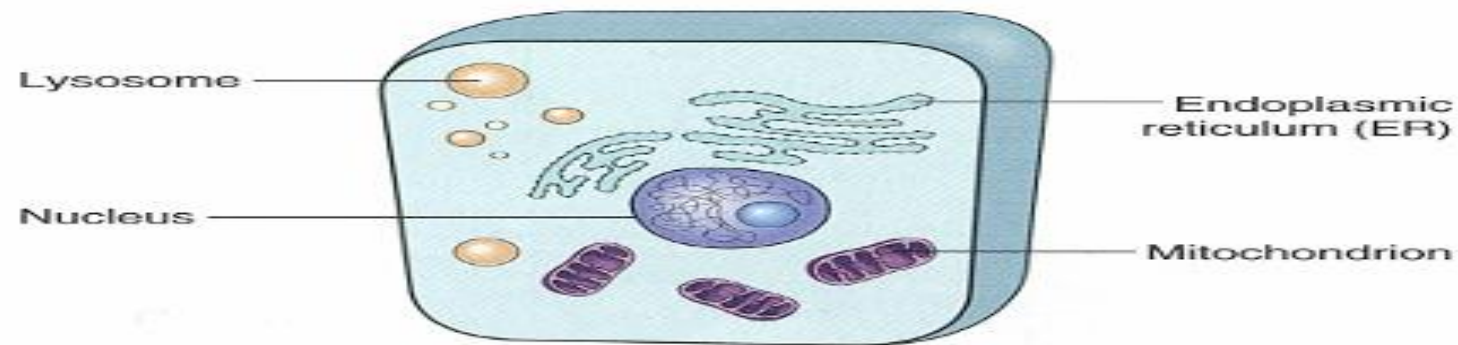
Defects  
in cell  
membrane

Large  
densities

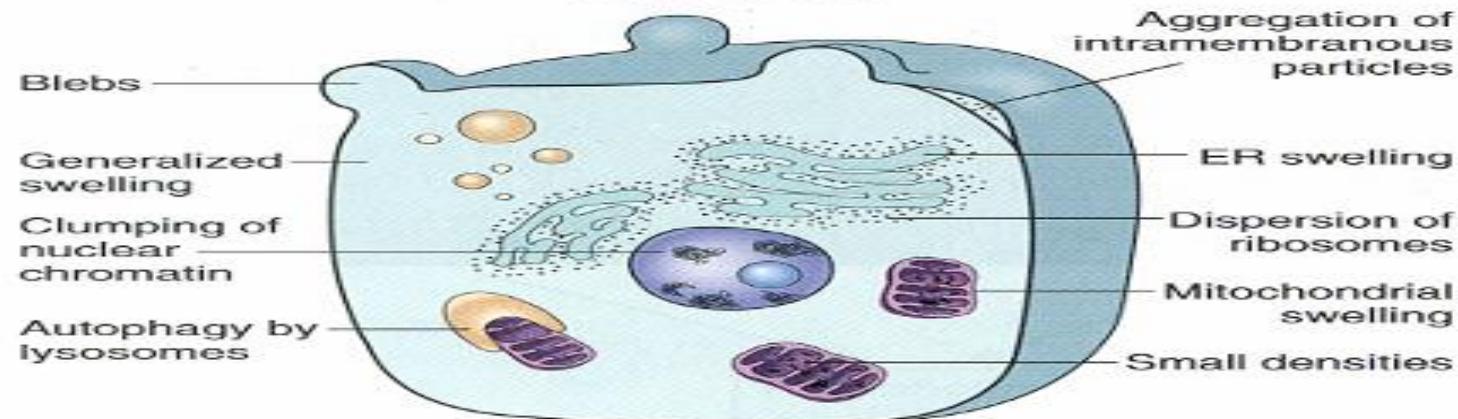
Mitochondrial  
swelling

C. Irreversible injury






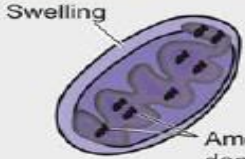


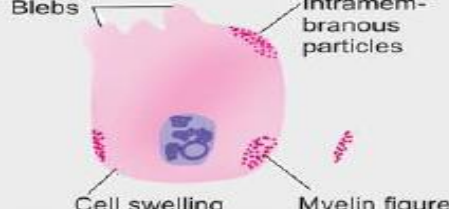












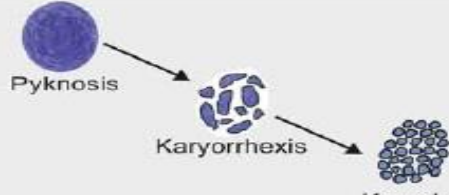
A. Normal cell



B. Reversible injury

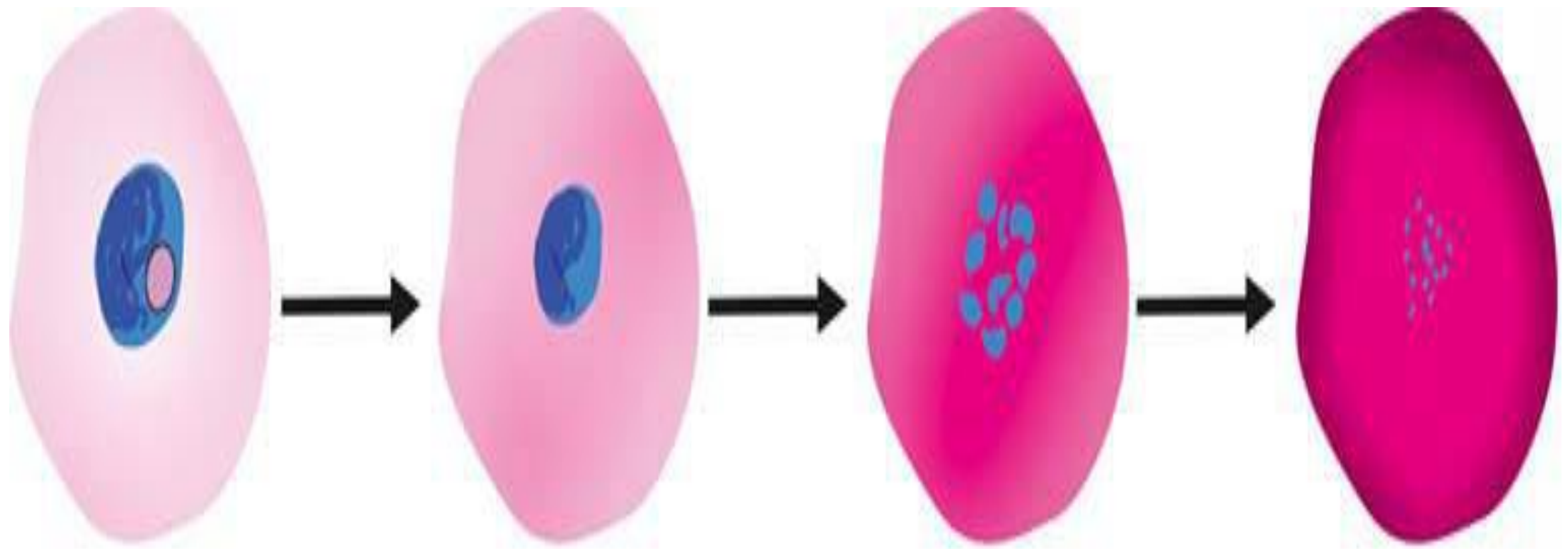


C. Irreversible injury

ORGANELLES IN NORMAL CELL	A, REVERSIBLE CELL INJURY	B, IRREVERSIBLE CELL INJURY
 1. MITOCHONDRIA	 Swelling Amorphous densities	 Swollen with vacuoles Large densities
 2. MEMBRANES	 Blebs Intramembranous particles Cell swelling Myelin figure	 Disruption Myelin figure
 3. RER AND RIBOSOMES	 Swelling Dispersed ribosomes	 Lysed Dispersed ribosomes
 4. LYSOSOMES	 Autophagy	 Swollen, ruptured
 5. CYTOSKELETON	 Aggregated	 Disrupted
 6. NUCLEUS	 Clumped chromatin	 Pyknosis Karyorrhexis Karyolysis

# Irreversible Injury – Nuclear Changes

- **Pyknosis**
  - Nuclear shrinkage and increased basophilia
- **Karyorrhexis**
  - Fragmentation of the pyknotic nucleus
- **Karyolysis**
  - Fading of basophilia of chromatin



A, Normal cell

B, Pyknosis

C, Karyorrhexis

D, Karyolysis

# Headings

- Introduction
- Definition
- Types of cell injury
- Etiology
- Mechanisms → 5
- Morphology

# POLLS 3

*Scan or Click to watch  
Cell Adaptation & Injury*



*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*





**Which of the following is the characteristic of irreversible injury on electron microscopy?**

- (a) Disruption of ribosomes
- (b) Amorphous densities in mitochondria
- (c) Swelling of endoplasmic reticulum
- (d) Cell swelling

**B**

**All of the following statements are true regarding reversible cell injury, except:**

- (a) Formation of amorphous densities in the mitochondrial matrix
- (b) Diminished generation of adenosine triphosphate (ATP).
- (c) Formation of blebs in the plasma membrane.
- (d) Detachment of ribosomes from the granular endoplasmic reticulum.

**A**

**Hypoxia decreases cellular levels of adenosine 5'-triphosphate (ATP) and inhibits the normal function of the plasma membrane ouabain-sensitive Na-K-ATPase pump. Which one of the following changes will result from decreased function of this membrane ion pump?**

### **Sodium Ion Changes**

- a. Decreased sodium ions inside the cell
- b. Decreased sodium ions outside the cell
- c. Increased sodium ions inside the cell
- d. Increased sodium ions outside the cell

### **Potassium Ion Changes**

- a. Decreased potassium ions outside the cell
- b. Increased potassium ions outside the cell
- c. Increased potassium ions outside the cell
- d. Increased potassium ions inside the cell

**C**

**Gross examination of the brain from an 89-year-old man with a long history of atherosclerotic disease reveals loss of brain substance that narrows the gyri and widens the sulci. Which one of the listed terms best describes this abnormality?**

- a. Atrophy**
- b. Hypertrophy**
- c. Hyperplasia**
- d. Metaplasia**

**A**



**Irreversible injury in cell is:**

- (a) Deposition of  $\text{Ca}^{++}$  in mitochondria
- (b) Swelling
- (c) Mitotic figure
- (d) Ribosomal detachment

**A**

# **First cellular change in hypoxia:**

- (a) Decreased oxidative phosphorylation in mitochondria**
- (b) Cellular swelling**
- (c) Alteration in cellular membrane permeability**
- (d) Clumping of nuclear chromatin**

**A**

**Cellular swelling with blebs and myelin figures are the changes seen in -**

- a) Reversible cell injury
- b) Irreversible cell injury
- c) Metaplasia
- d) Anaplasia

**A**

**Not an irreversible injury?**

- a) Pyknosis
- b) Karyorrhexis
- c) Karyolysis
- d) Bleb formation

**D**



# **TYPES OF CELLS**

1. Labile cells
2. Stable cells
3. Permanent cells

# Labile

## Continuous regeneration from stem cells (self-renewal)

- a) Hematopoietic cells in bone marrow
- b) Surface epithelia – skin, oral cavity, vagina, cervix
- c) Duct epithelia – salivary glands, pancreas, biliary tract
- d) Mucosae – GIT, uterus, fallopian tubes, urinary bladder

# Stable

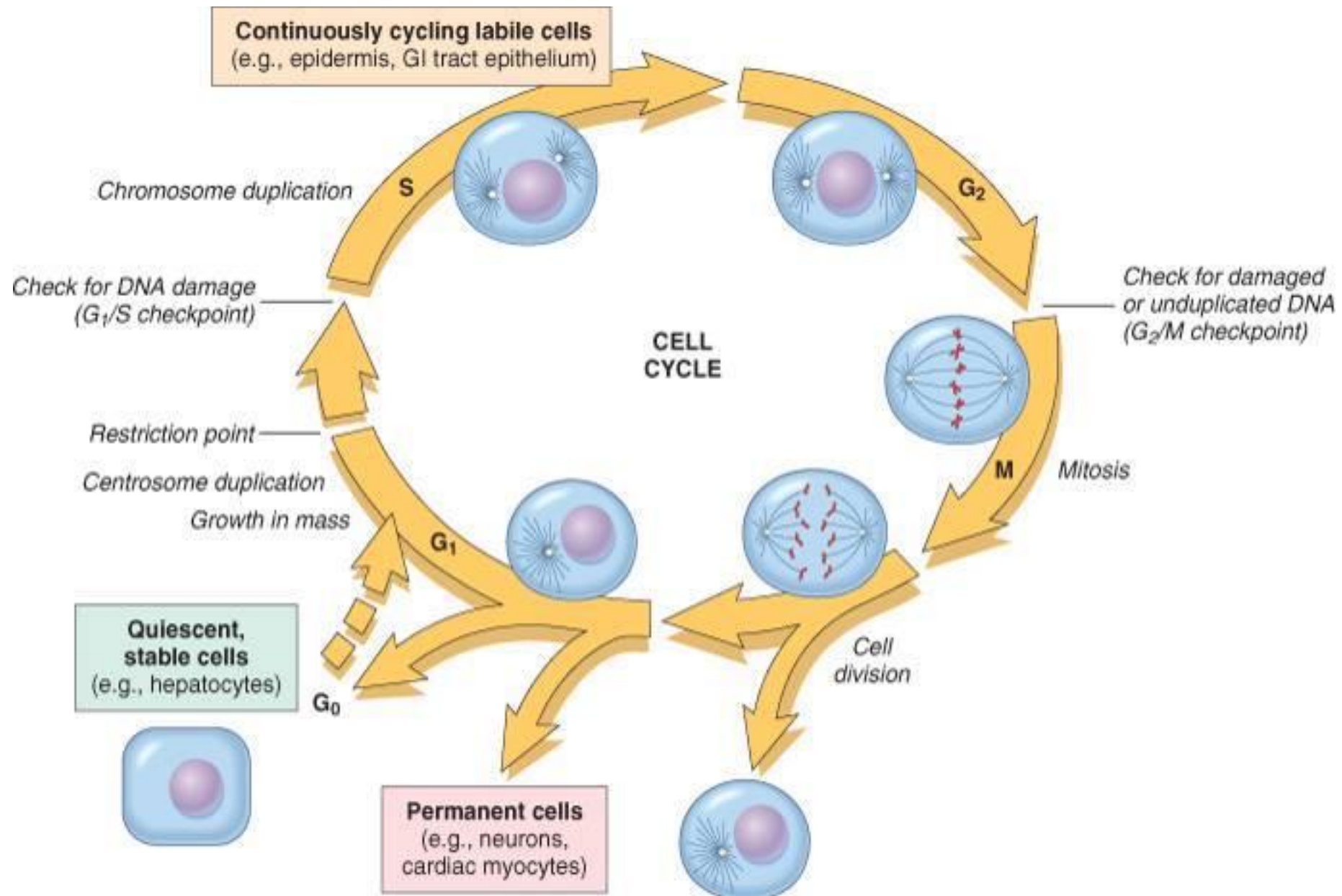
## Regeneration as response to injury

- a) Parenchyma – liver, pancreas, renal tubules
- b) Mesenchymal cells, endothelium

# Permanent

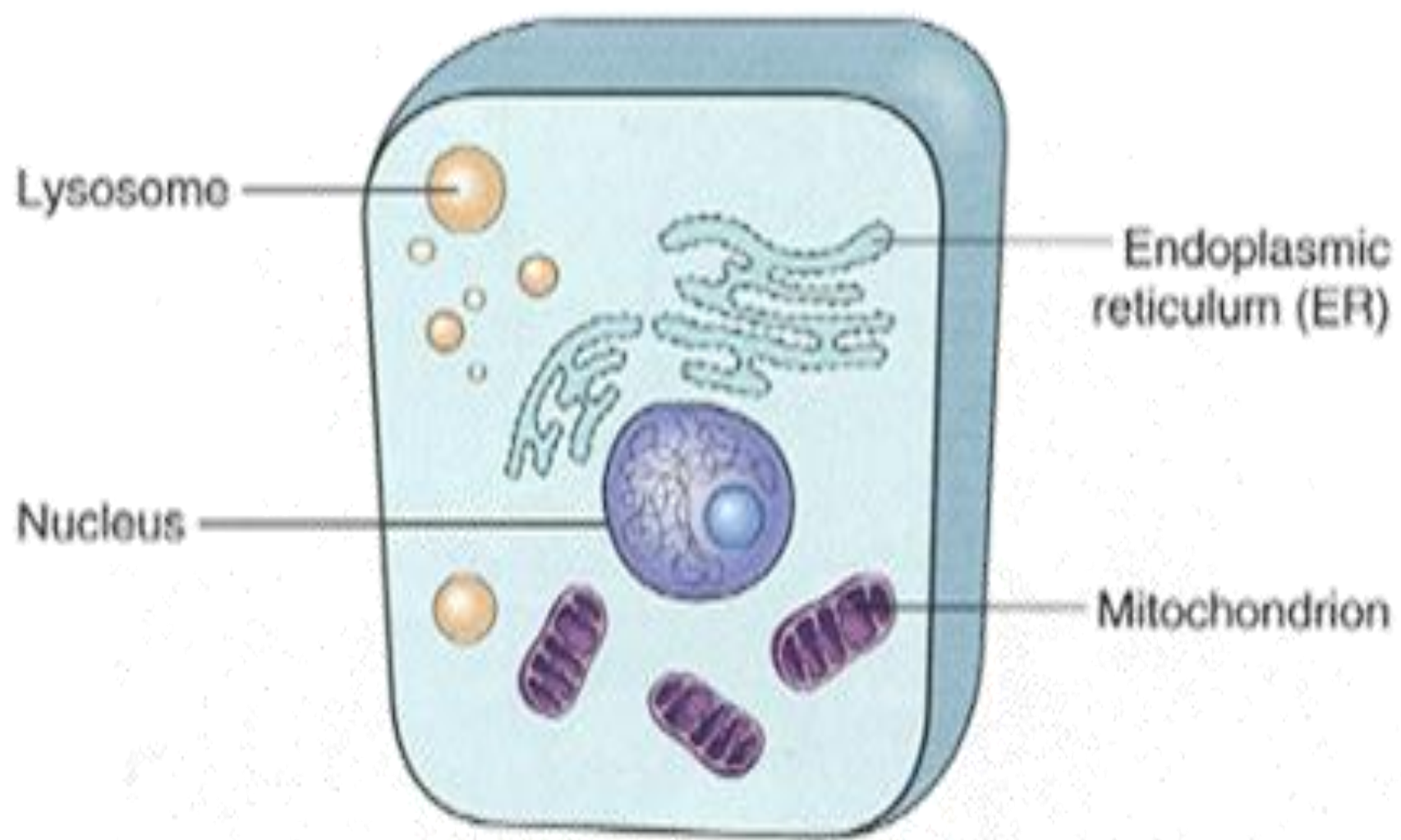
**Nonproliferative in postnatal life**

- a) Neurons
- b) Cardiomyocytes



# INTRODUCTION

- **Cells** are the **structural and functional units** of tissues and organs.
- Normal cells have a fairly narrow range of function or steady state: **Homeostasis**



A. Normal cell

**Normally cells in homeostasis**



**Physiological and pathological stress**



**Cellular adaptation** (reversible on withdrawal of stimulus)



**If the irritant stimulus persists for long time**



**Cell injury**



**Reversible cell injury**

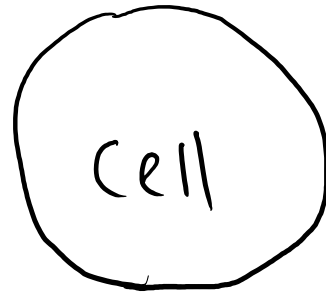


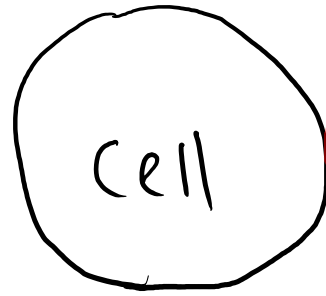
**Irreversible cell injury (Cell death)**

**-Apoptosis**

**-Necrosis**



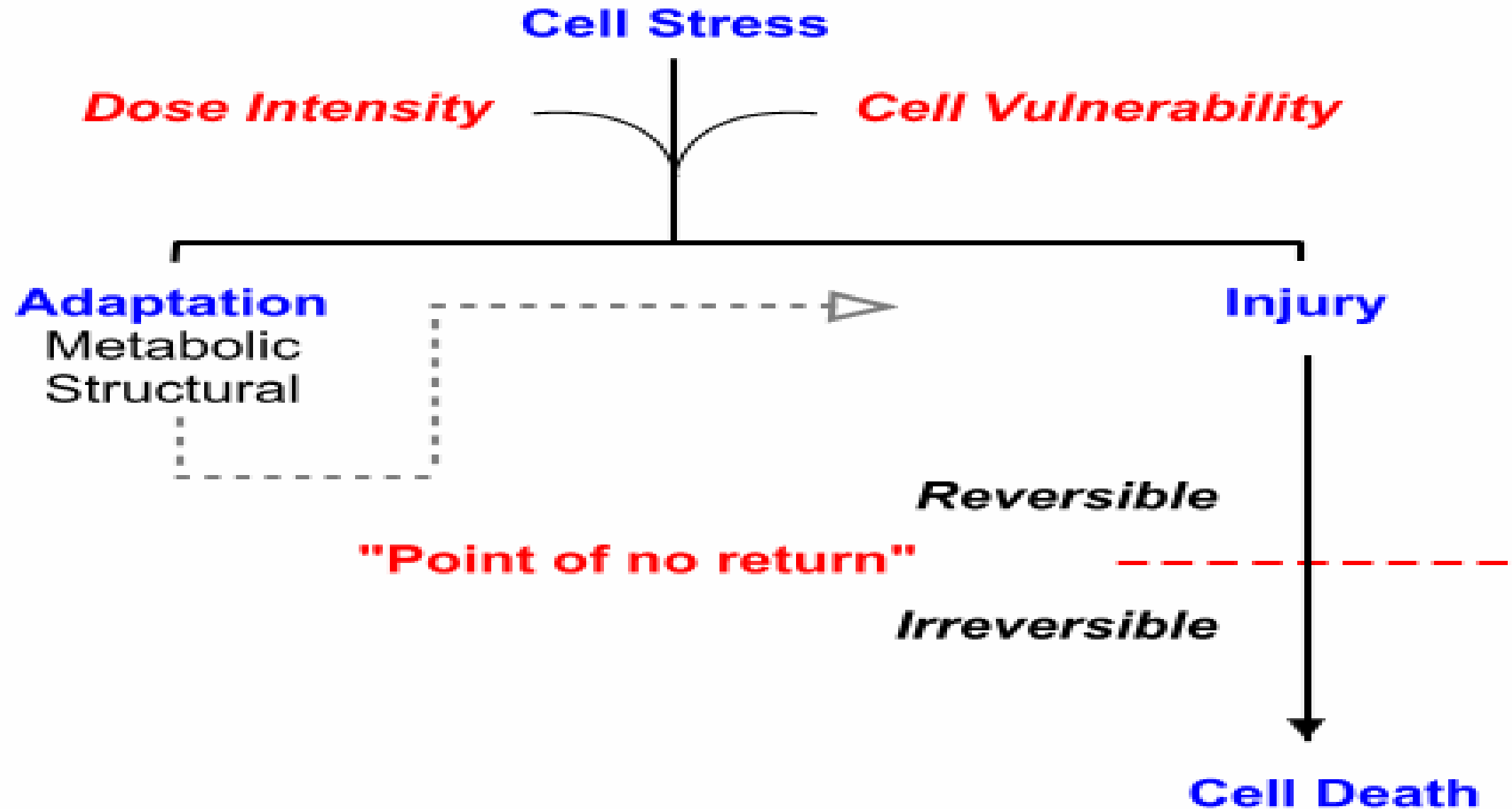




STRESS  
(physiological or  
pathological)

- **Cell injury** results when cells are stressed so severely that they are **no longer able to adapt**
- i.e., when the limits of adaptive response to a stimulus are exceeded, cell injury occurs.

- **Cell injury is reversible up to a certain point, but if the stimulus persists or is severe enough from the beginning, the cell reaches a “point of no return” and suffers irreversible injury and ultimate cell death.**



- **Adaptation, reversible injury and irreversible injury & cell death** are stages of progressive impairment of the cell's normal function and structure.

# **CELL DEATH**

**DR. PRIYANKA SACHDEV, MD**

# CELL DEATH

- Apoptosis
- Necrosis



# Apoptosis

# **OVERVIEW**

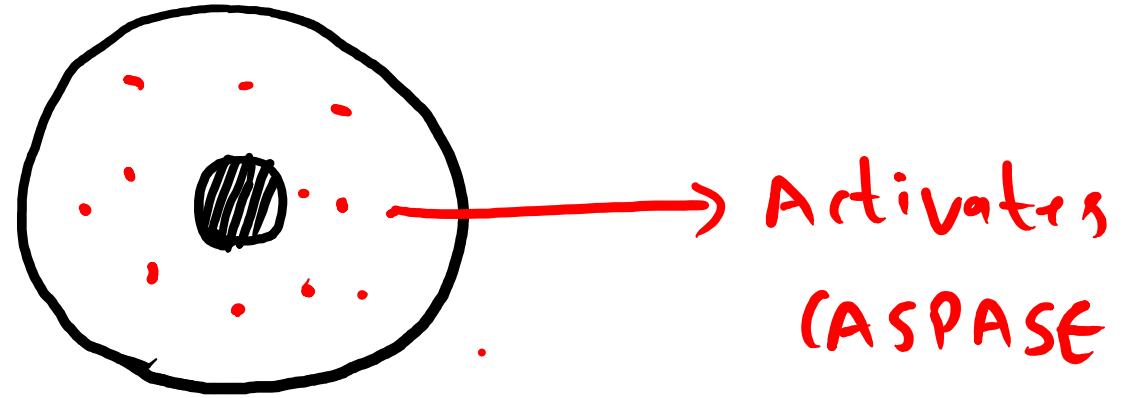
- **Definition**
- **Types**
- **Mechanisms**
- **Morphological changes in apoptosis**
- **Diagnosis of Apoptosis**
- **Differences from necrosis**

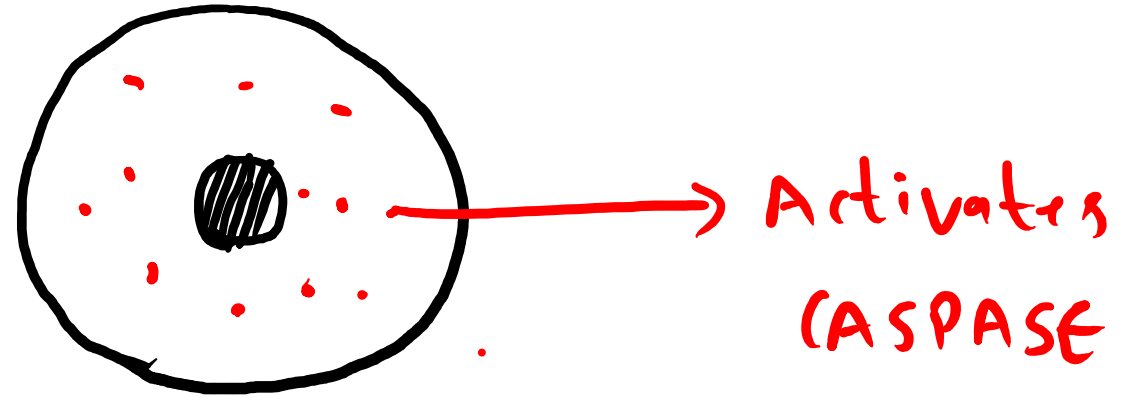
# Definition

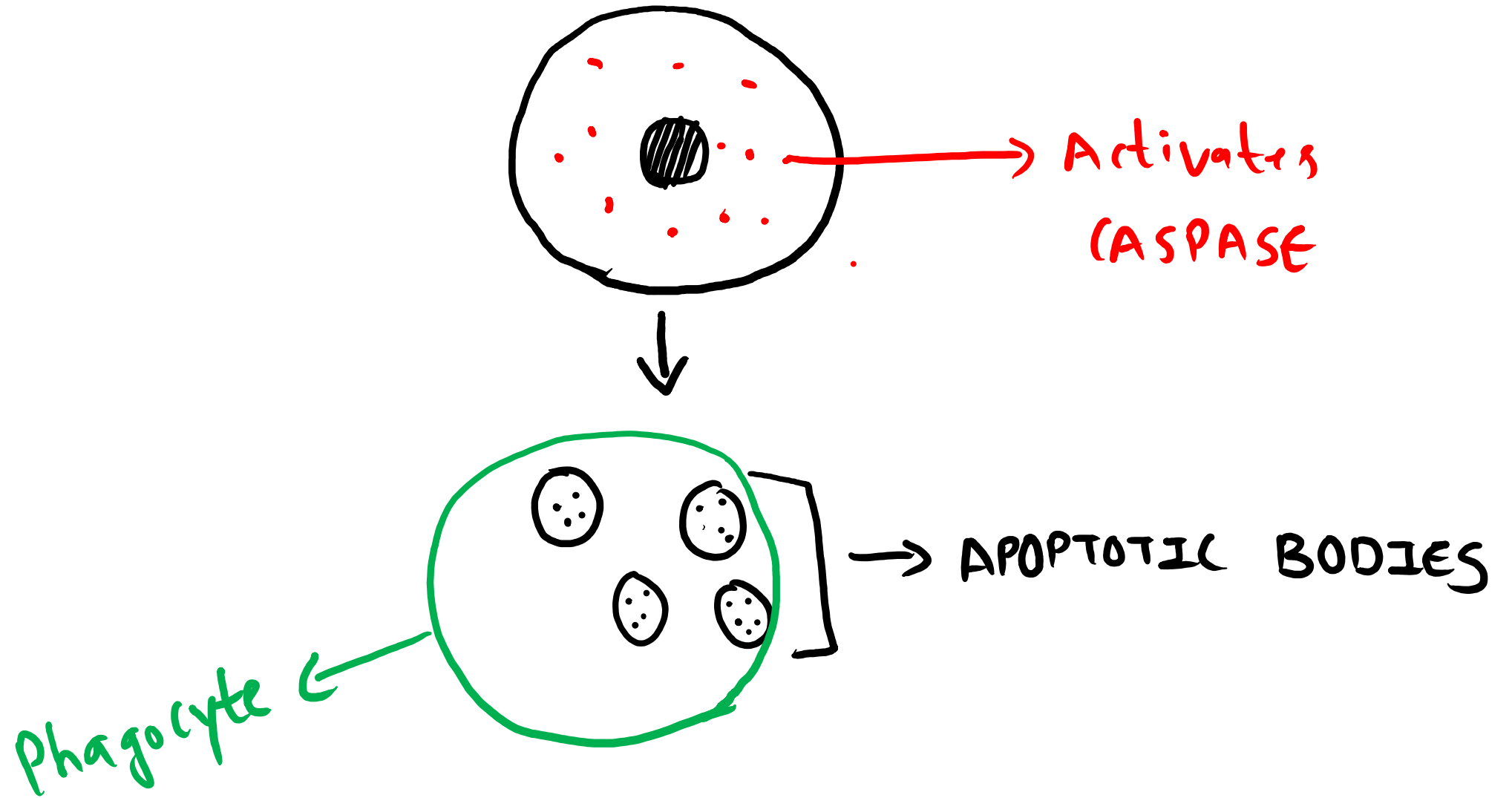
**CELL SUICIDE**

# Definition

- It is a pathway of **cell death** that is induced by a **tightly regulated intracellular program** in which cells destined to die activate enzymes (**caspase**) degrade the cells own nuclear DNA and cytoplasmic proteins.
- The cell is phagocytosed
- There is no leakage outside
- So there is no inflammation







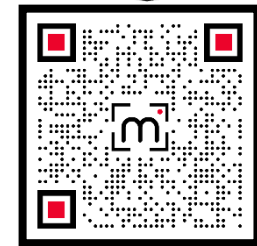
# Definition

- It is a pathway of **cell death** that is induced by a **tightly regulated intracellular program** in which cells destined to die activate enzymes (**caspase**) degrade the cells own nuclear DNA and cytoplasmic proteins.
- The cell is phagocytosed
- There is no leakage outside
- So there is no inflammation



- It is the **way of elimination** of unwanted cells and those cells which are damaged beyond repair capacity of cell.

*Click or Scan QR code to join  
Telegram group discussion*



- Apoptosis generally involves **single cell** in contrast to necrosis that usually involve a group of cells.

- It is the ‘ **programmed cell death**’.
- It is **genetically programmed**.
- It is an **energy dependent** process.

# POLLS

*Scan or Click to watch  
Cell Adaptation & Injury*



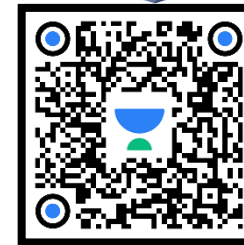
*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*



# **Central to apoptosis is the utilization of**

- **a) Nitrous oxide**
- **b) Adenyl cyclase**
- **c) Caspases**
- **d) c-AMP**

# **Central to apoptosis is the utilization of -**

- a) Nitrous oxide
- b) Adenyl cyclase
- **c) Caspases**
- d) c-AMP

# **OVERVIEW**

- **Definition**
- **Types**
- **Mechanisms**
- **Morphological changes in apoptosis**
- **Diagnosis of Apoptosis**
- **Differences from necrosis**

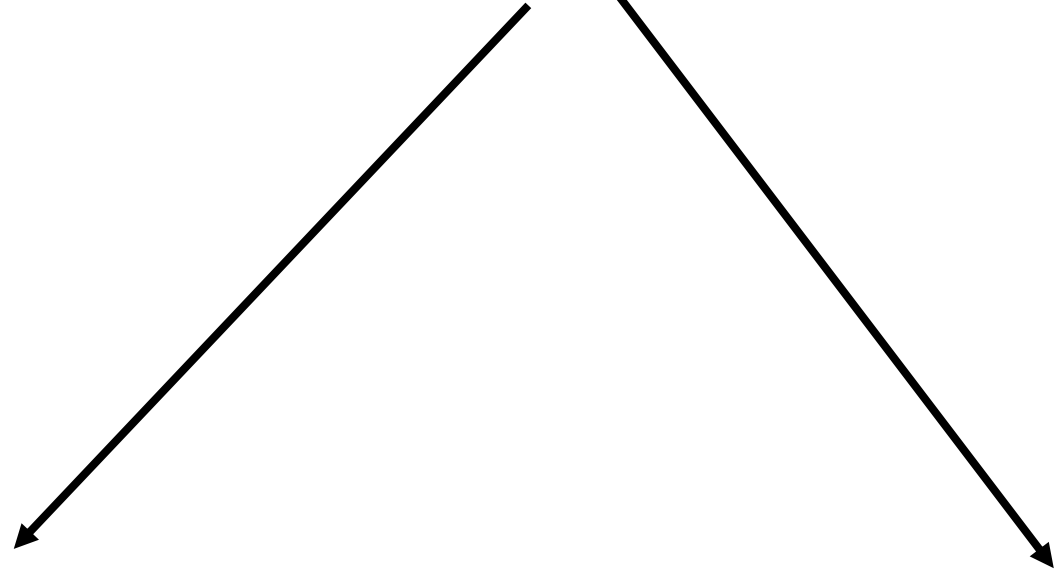
# **TYPES**

**Apoptosis may be of two types →**

- **A) Physiological → Programmed cell death**
- **B) Pathological → Unprogrammed cell death**



**APOPTOSIS**



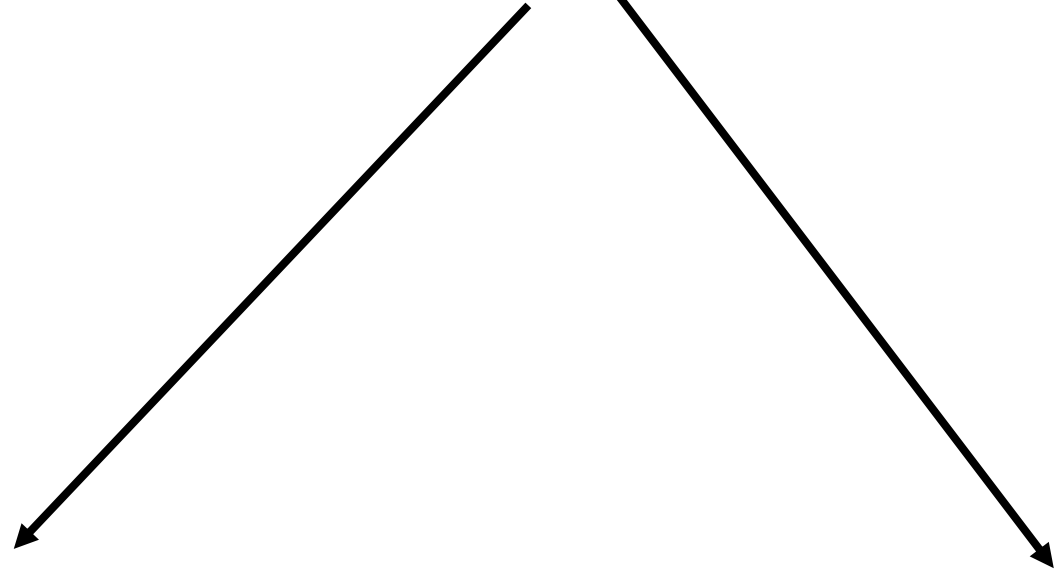
**Physiological**

**Pathological**

# **Physiological causes**

1. Embryogenesis
2. Elimination of potentially self reacting lymphocytes.
3. Hormone dependent involution of uterus and breast.
4. Death of cells that have completed their functions

**APOPTOSIS**



**Physiological**

**Pathological**

# Pathological Causes

- 1. Cell death in tumours exposed to chemotherapeutic agents.
- 2. Progressive depletion of CD4+T cells in the pathogenesis of AIDS.
- 3. Cell death in viral infections e.g. formation of Councilman bodies in viral hepatitis.

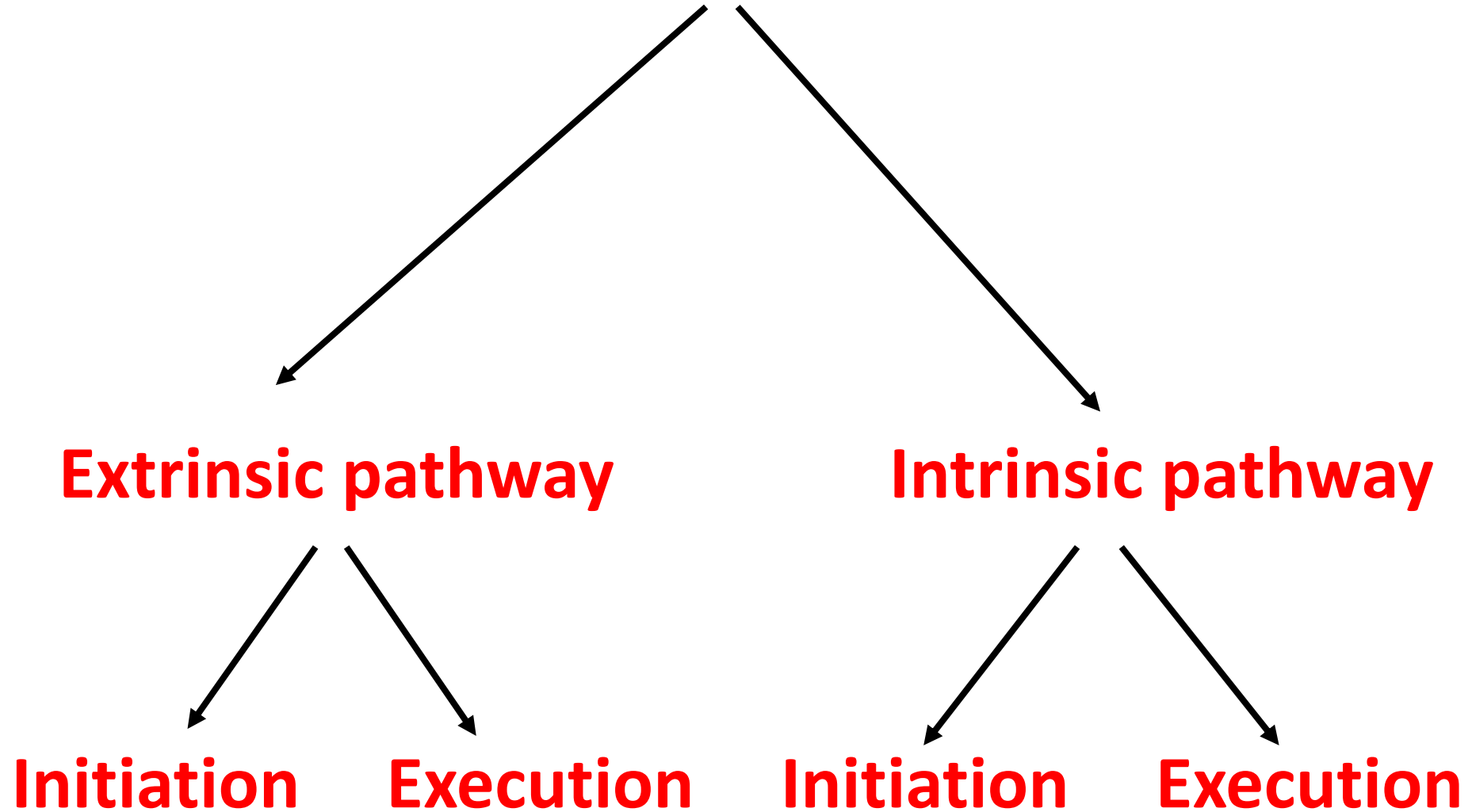
# **OVERVIEW**

- **Definition**
- **Types**
- **Mechanisms**
- **Morphological changes in apoptosis**
- **Diagnosis of Apoptosis**
- **Differences from necrosis**

# Mechanism

- Apoptosis can be induced through two distinct but convergent pathways.
1. **Extrinsic pathway** – it is initiated by extracellular stimulus with help of specific receptors called **death receptors**
  2. **Intrinsic pathway** – it is result of increased **mitochondrial membrane** permeability and release of pro- apoptotic markers like cytochrome C into the cytoplasm.

# Mechanism



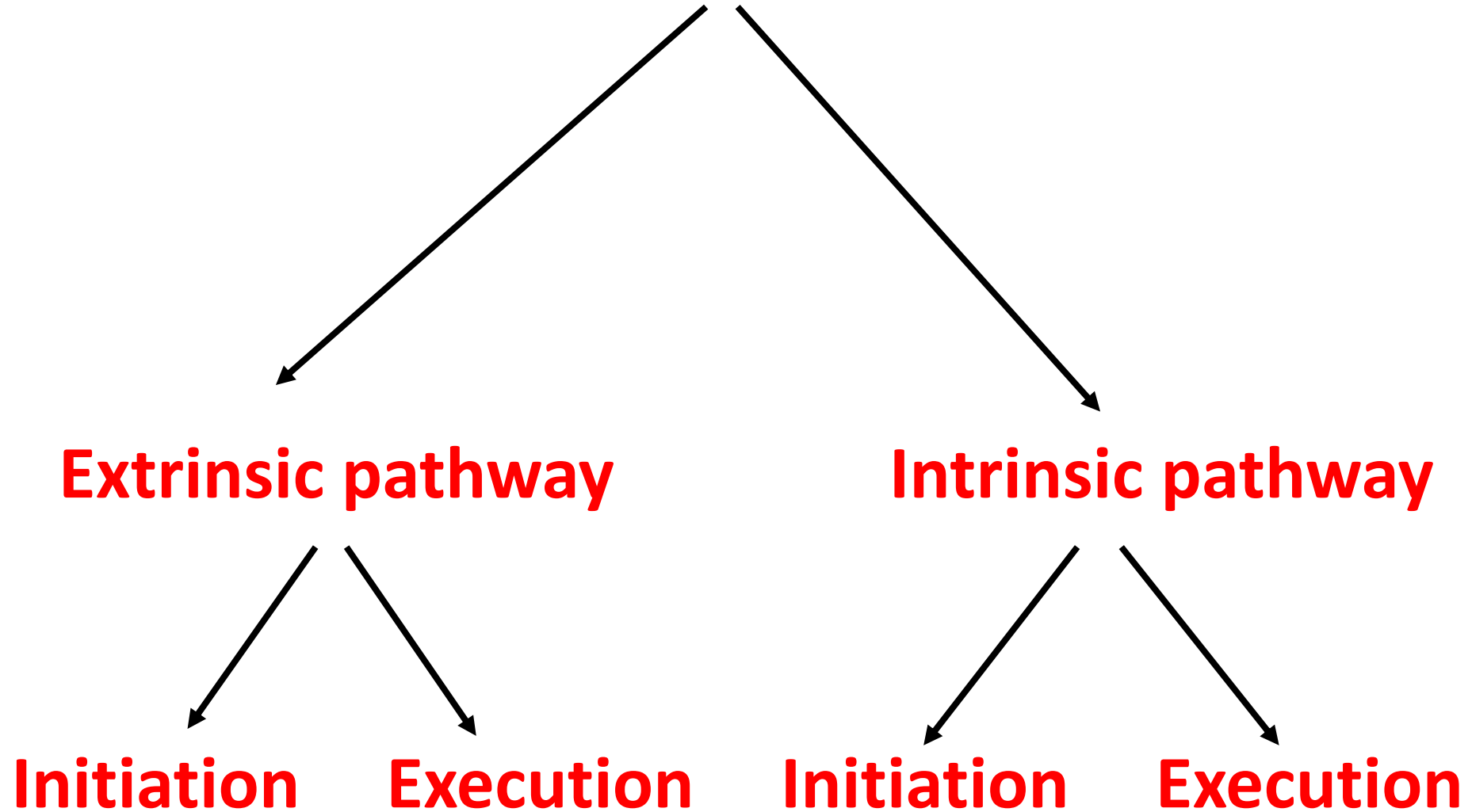
# Phases

Apoptosis can be divided into two phases:

- 1. Initiation phase** : starts with stimulus ( either extrinsic or intrinsic) and consist of catabolic activation of caspase like 8 or 9.
- 2. Execution phase**: executioner caspases act to cause cell death.



# Mechanism

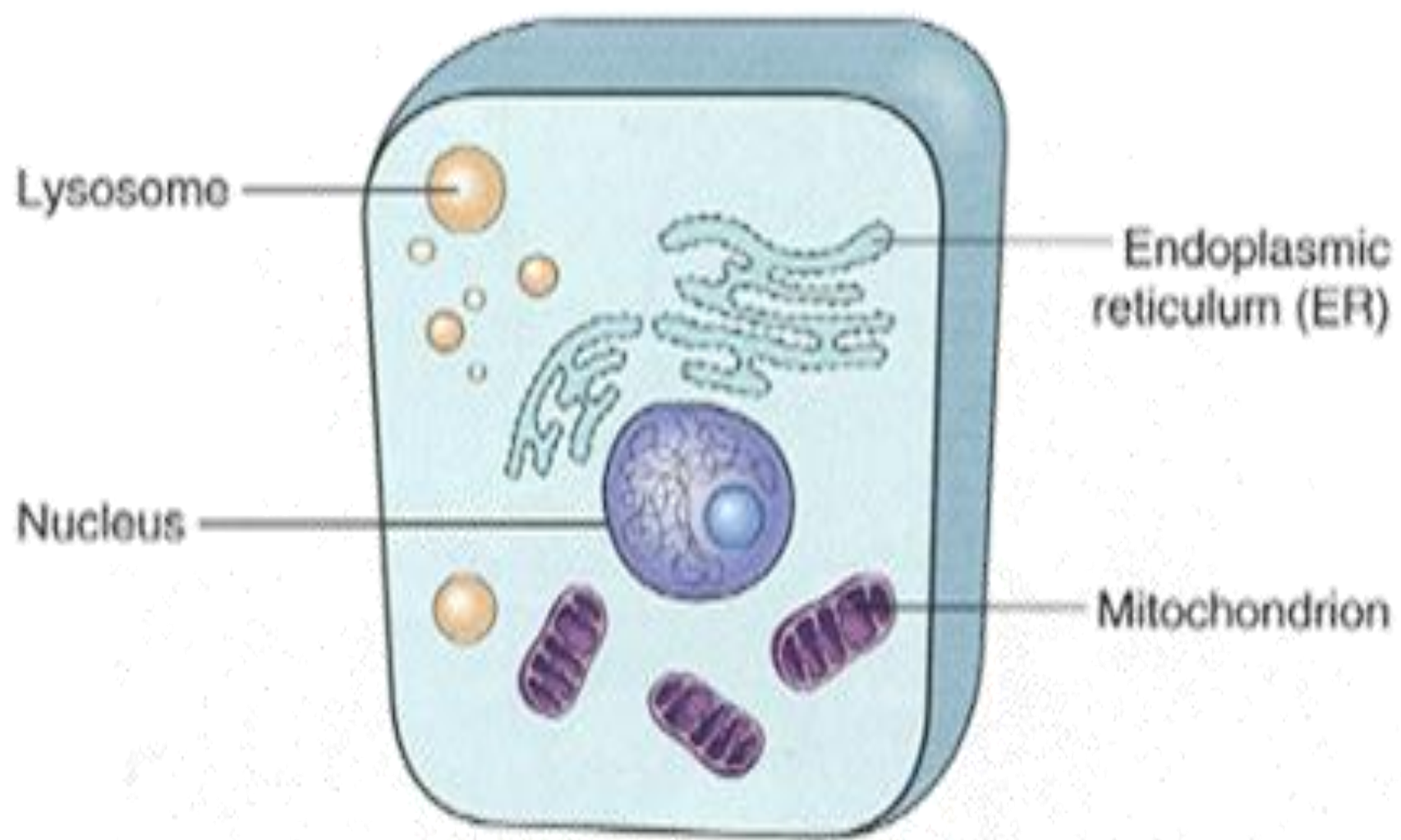


# Extrinsic pathway → Initiation phase

- It is initiated through specific receptors called **death receptors**

1. Fas protein (CD95)

2. TNF receptors



A. Normal cell

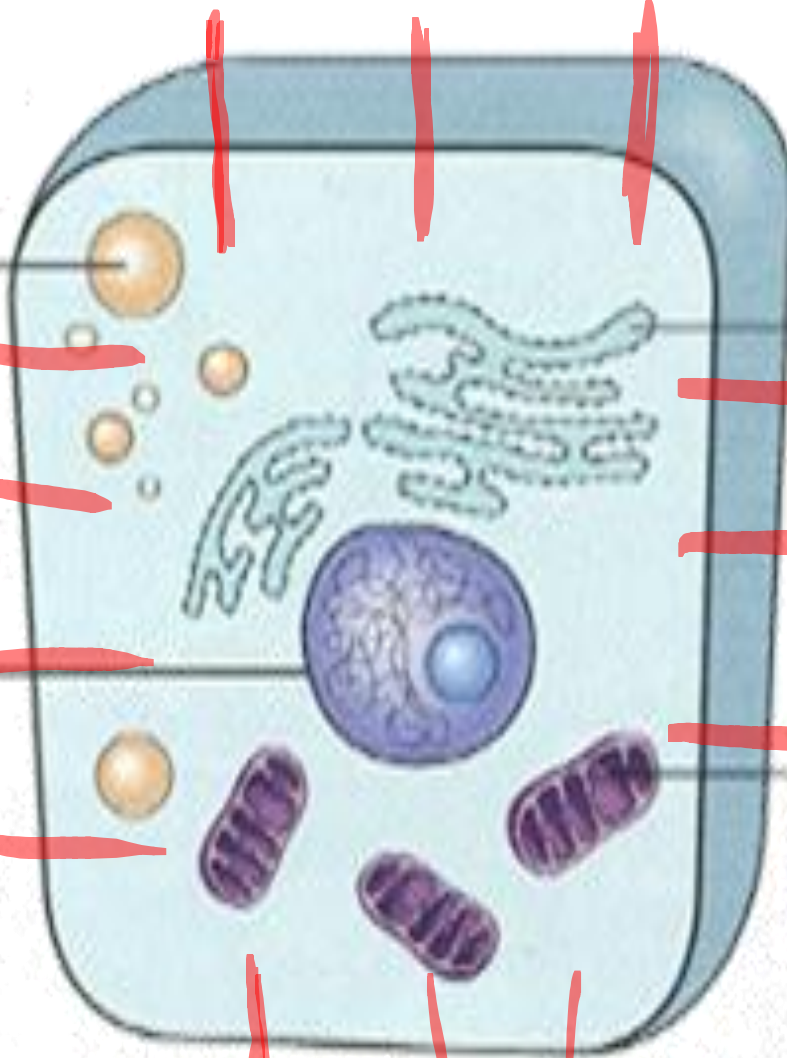
Lysosome

Endoplasmic  
reticulum (ER)

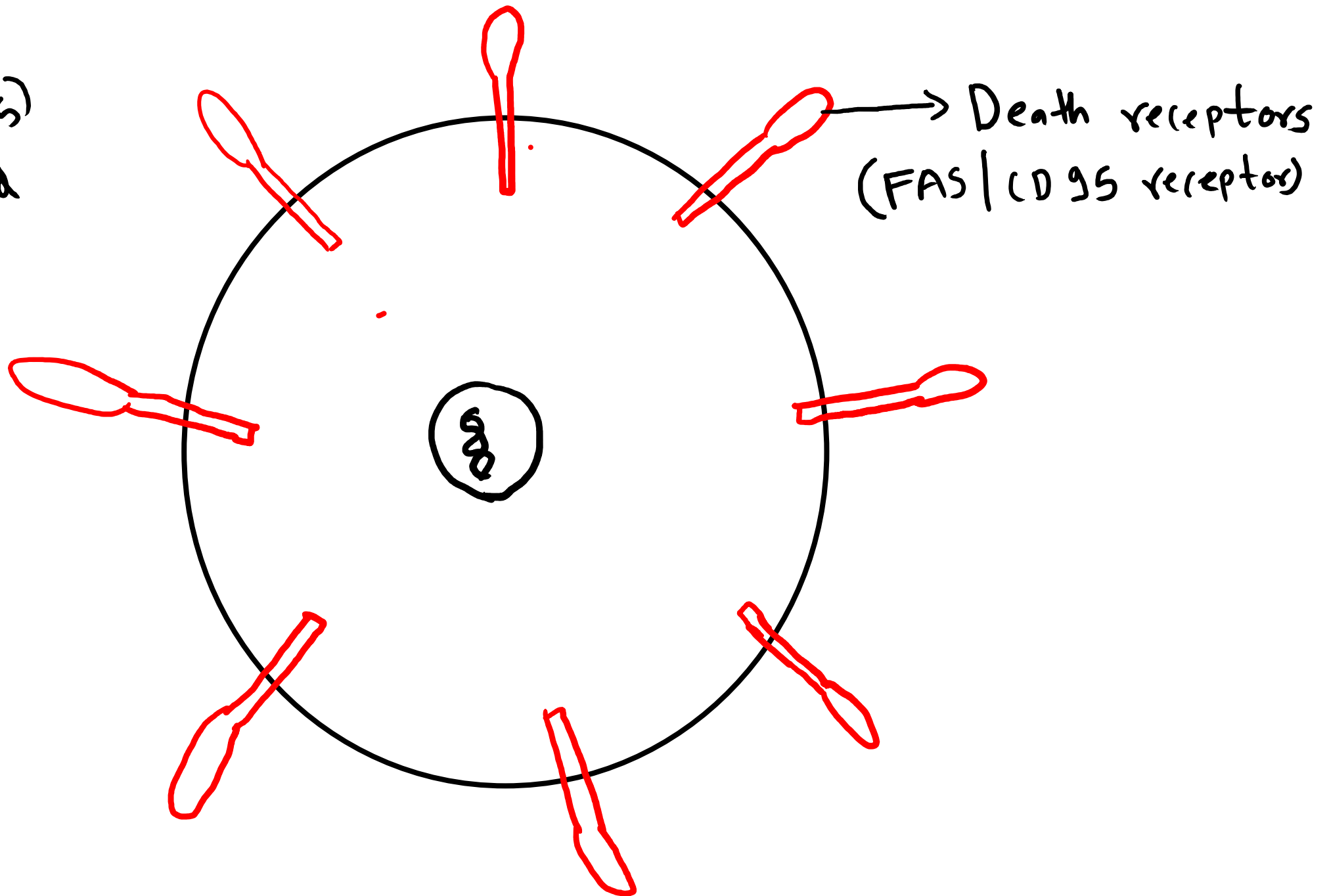
Nucleus

Mitochondrion

A. Normal cell

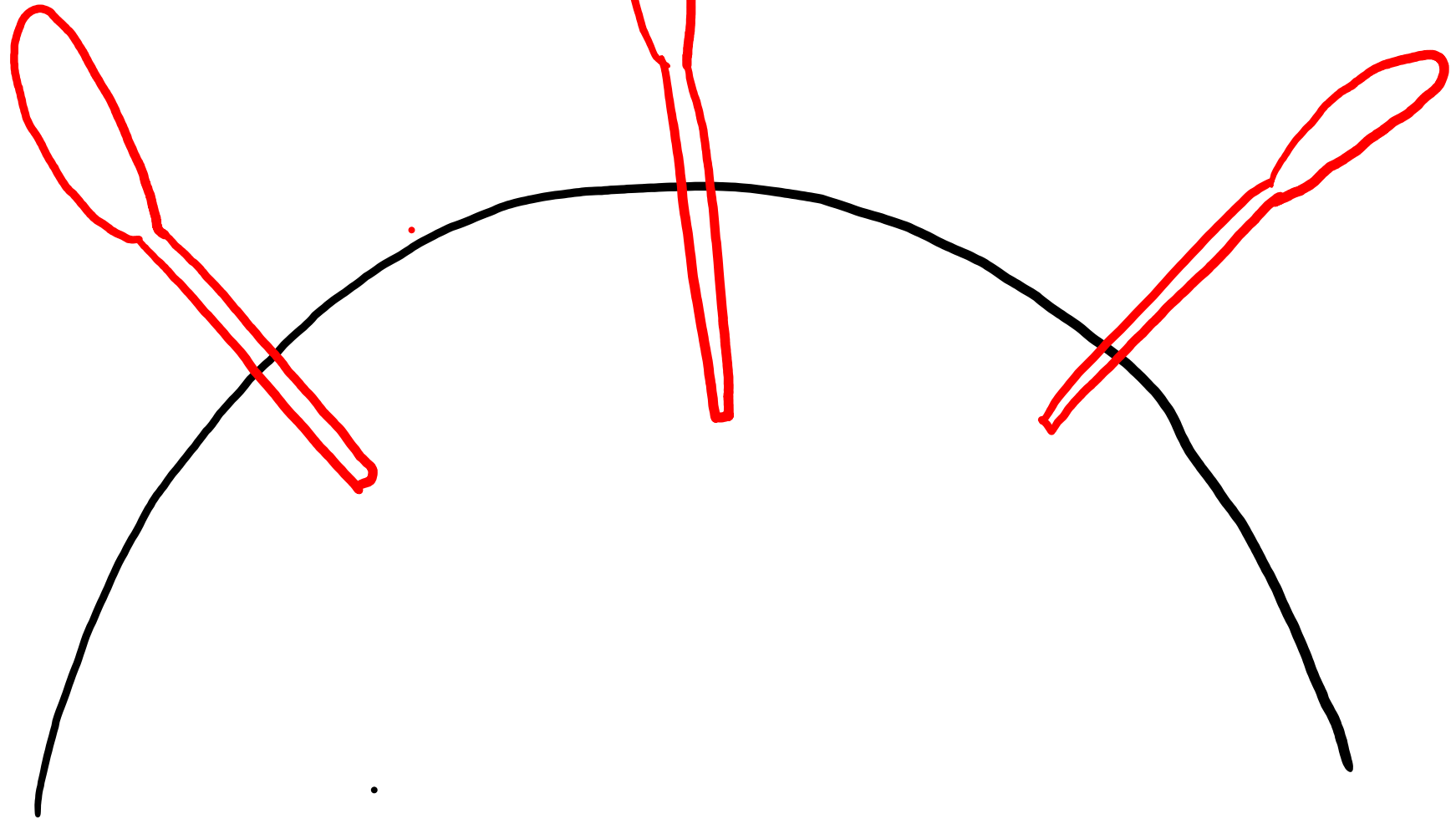


 FAS (CD95)  
Ligand

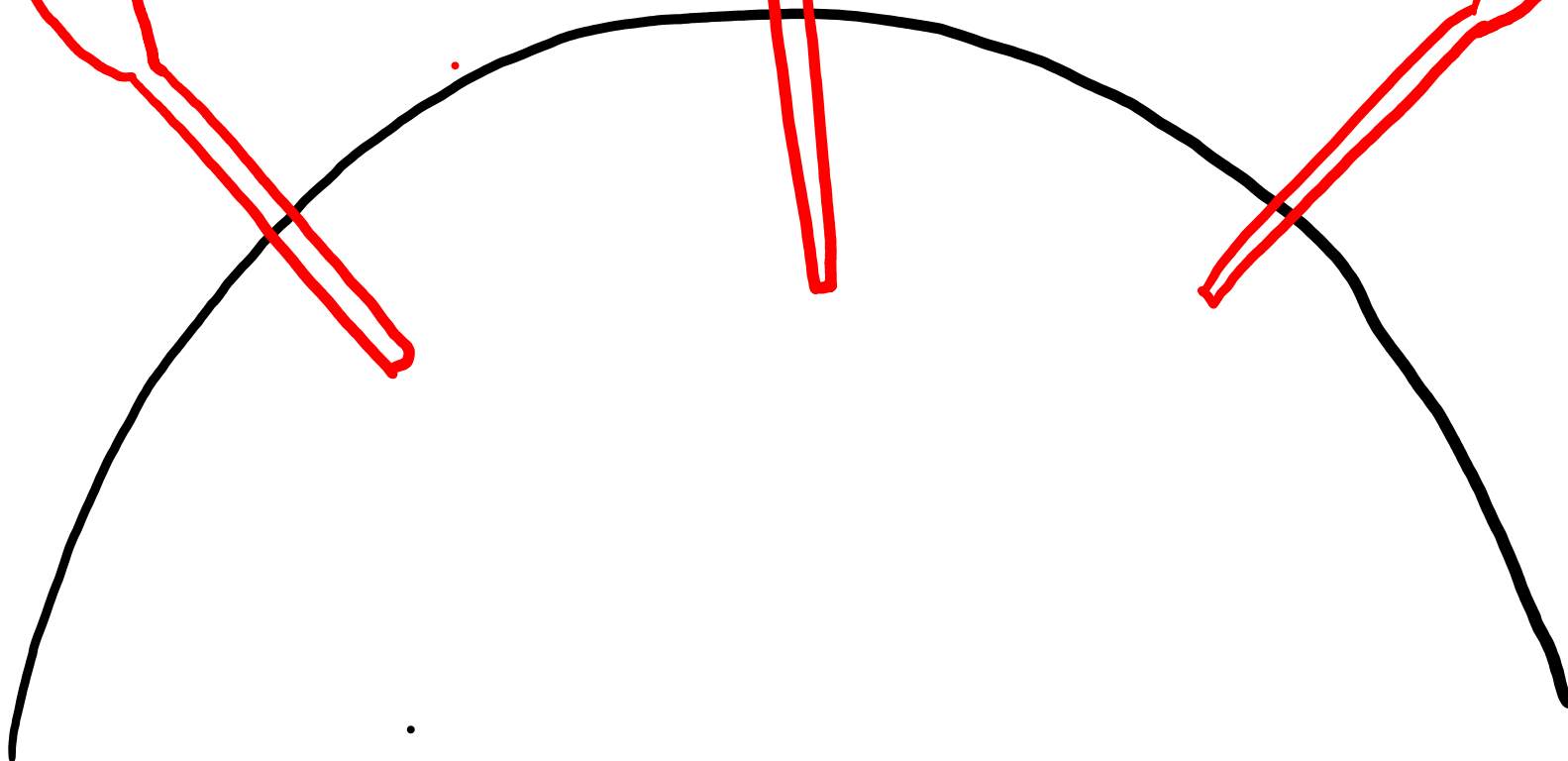
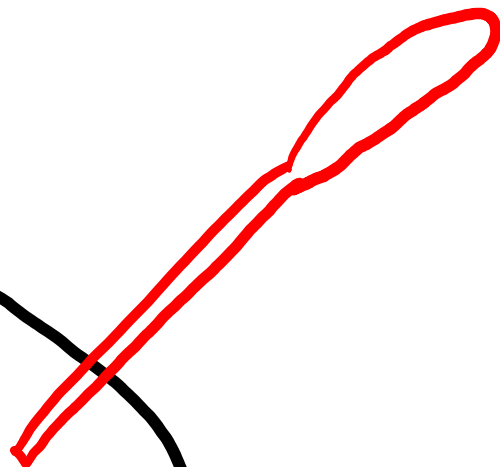
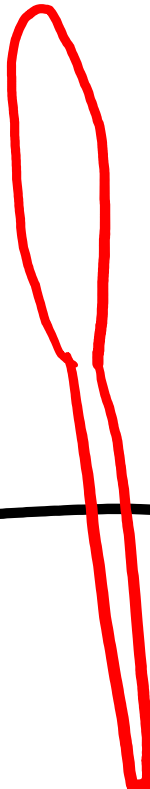
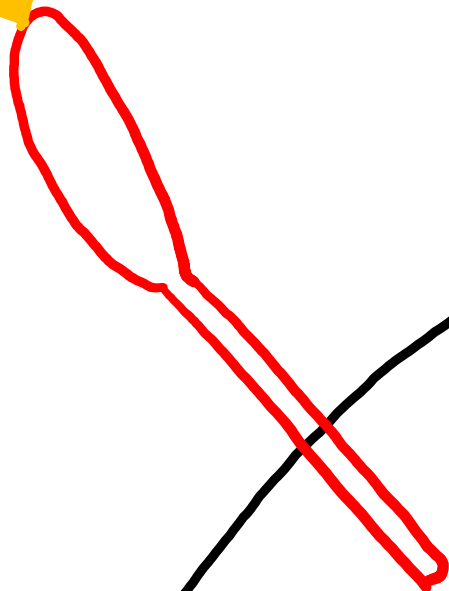


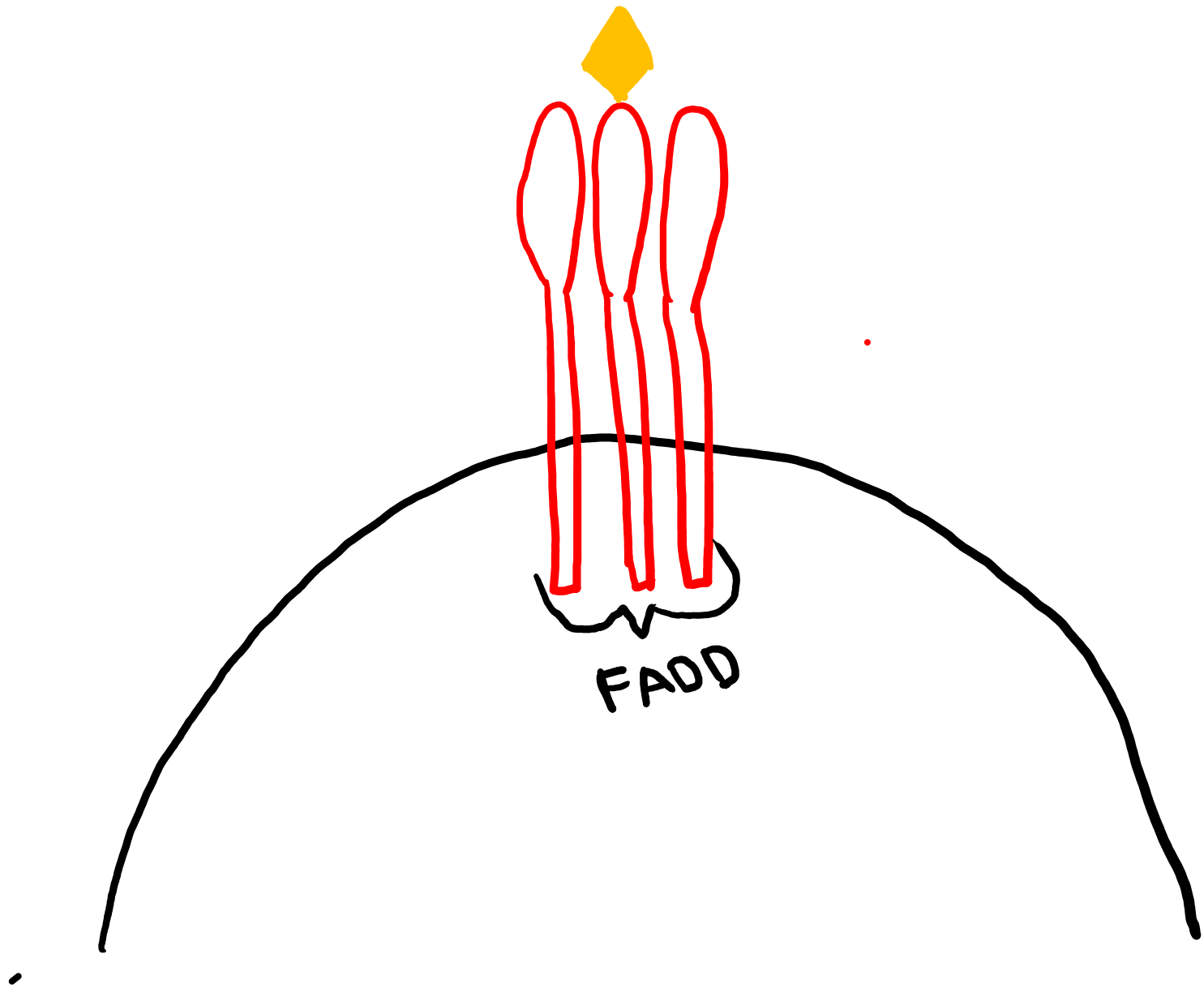
 FAS (CD 95)

→ Death receptors  
(FAS / CD 95 receptor)

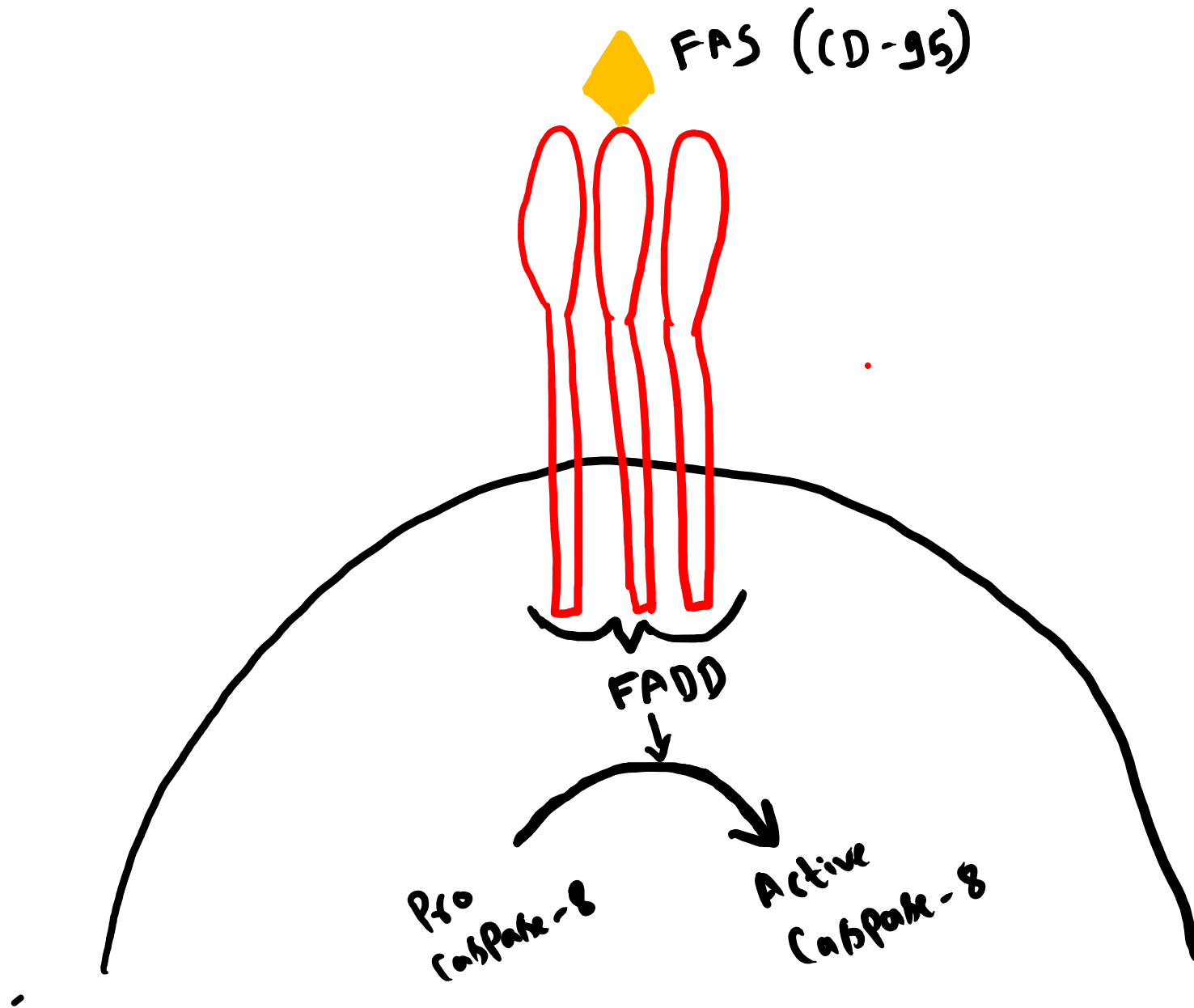


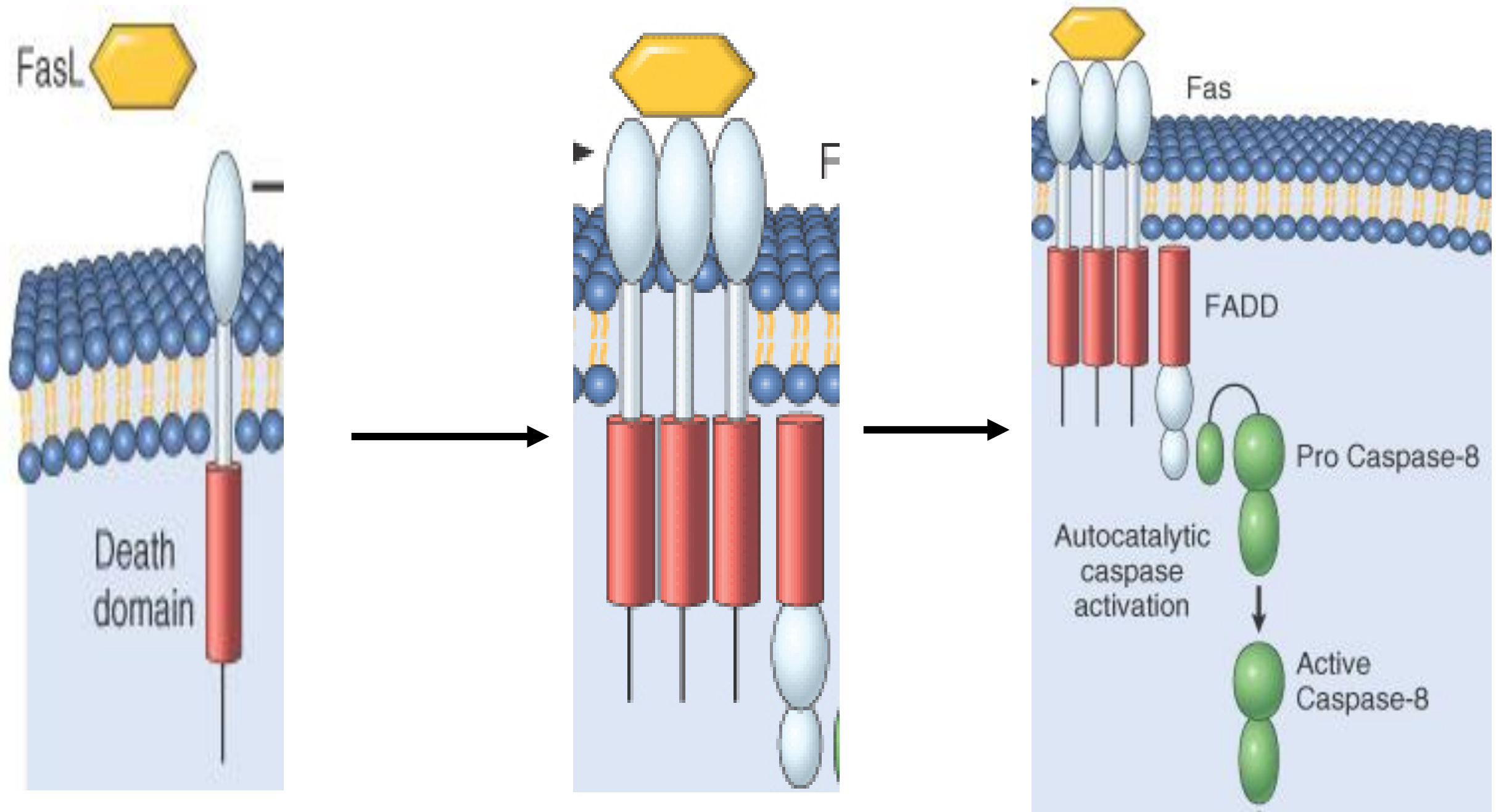
FAS (CD 95)











**Fas protein (CD95)**



**Fas receptor (Death receptor)**



**Multiple Fas proteins come together**



**Cytoplasmic death domains combine to form a death domain**  
**FADD**



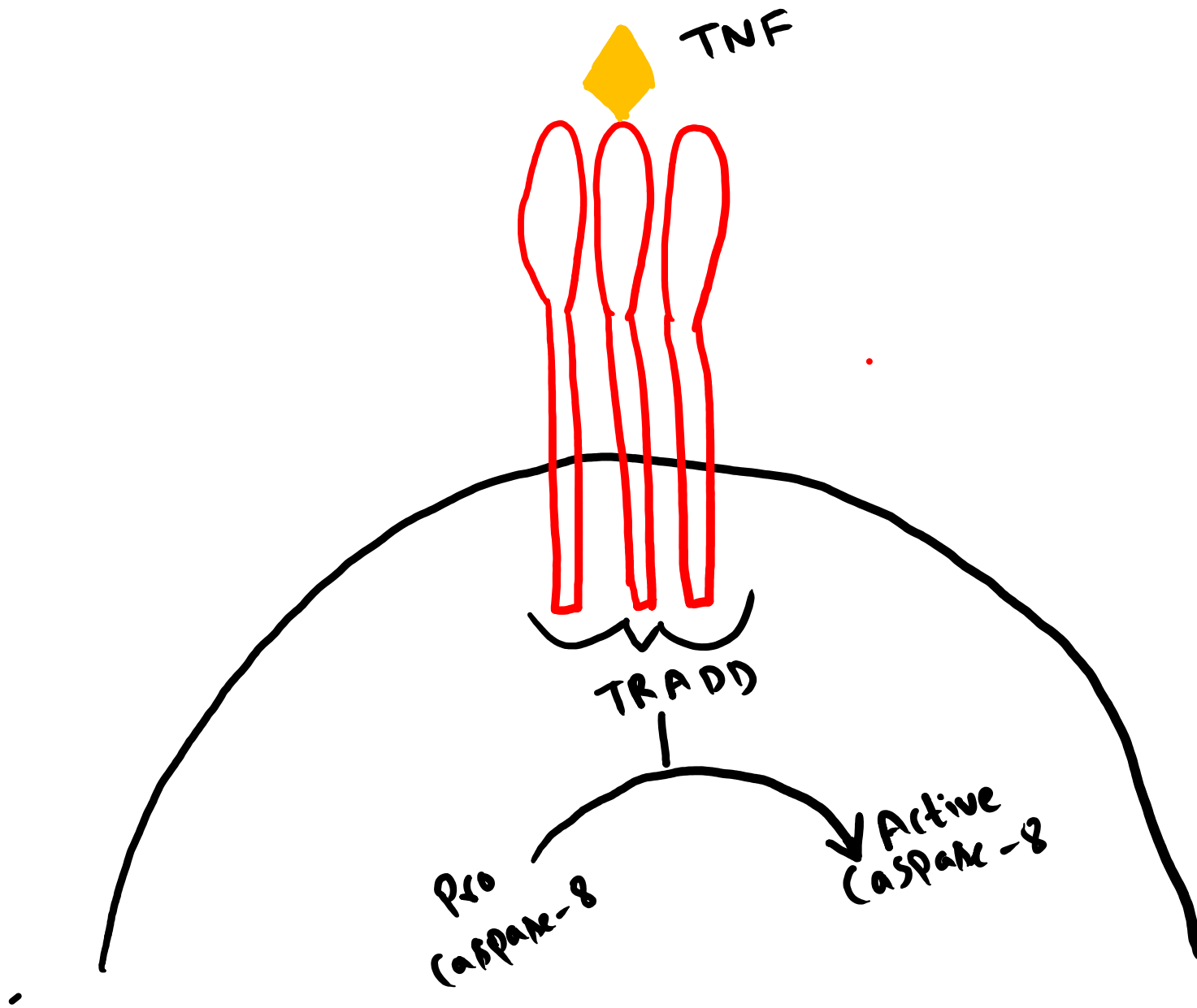
**Activate pro- caspsase 8 to active caspase 8**

# Extrinsic pathway → Initiation phase

- It is initiated through specific receptors called **death receptors**

1. Fas protein (CD95)

2. TNF receptors



**TNF**



**TNF receptor**



**Multiple Fas proteins come together**



**Cytoplasmic death domains combine to form a death domain**

**TRADD**



**Active pro- caspsase 8 to active caspase 8**

**Mechanism**

```
graph TD; Mechanism --> Extrinsic[Extrinsic pathway]; Mechanism --> Intrinsic[Intrinsic pathway]; Extrinsic --> Initiation1[Initiation]; Extrinsic --> Execution1[Execution]; Intrinsic --> Initiation2[Initiation]; Intrinsic --> Execution2[Execution];
```

**Extrinsic pathway**

**Intrinsic pathway**

**Initiation**

**Execution**

**Initiation**

**Execution**

# Mechanism

**Extrinsic pathway**

**Intrinsic pathway**

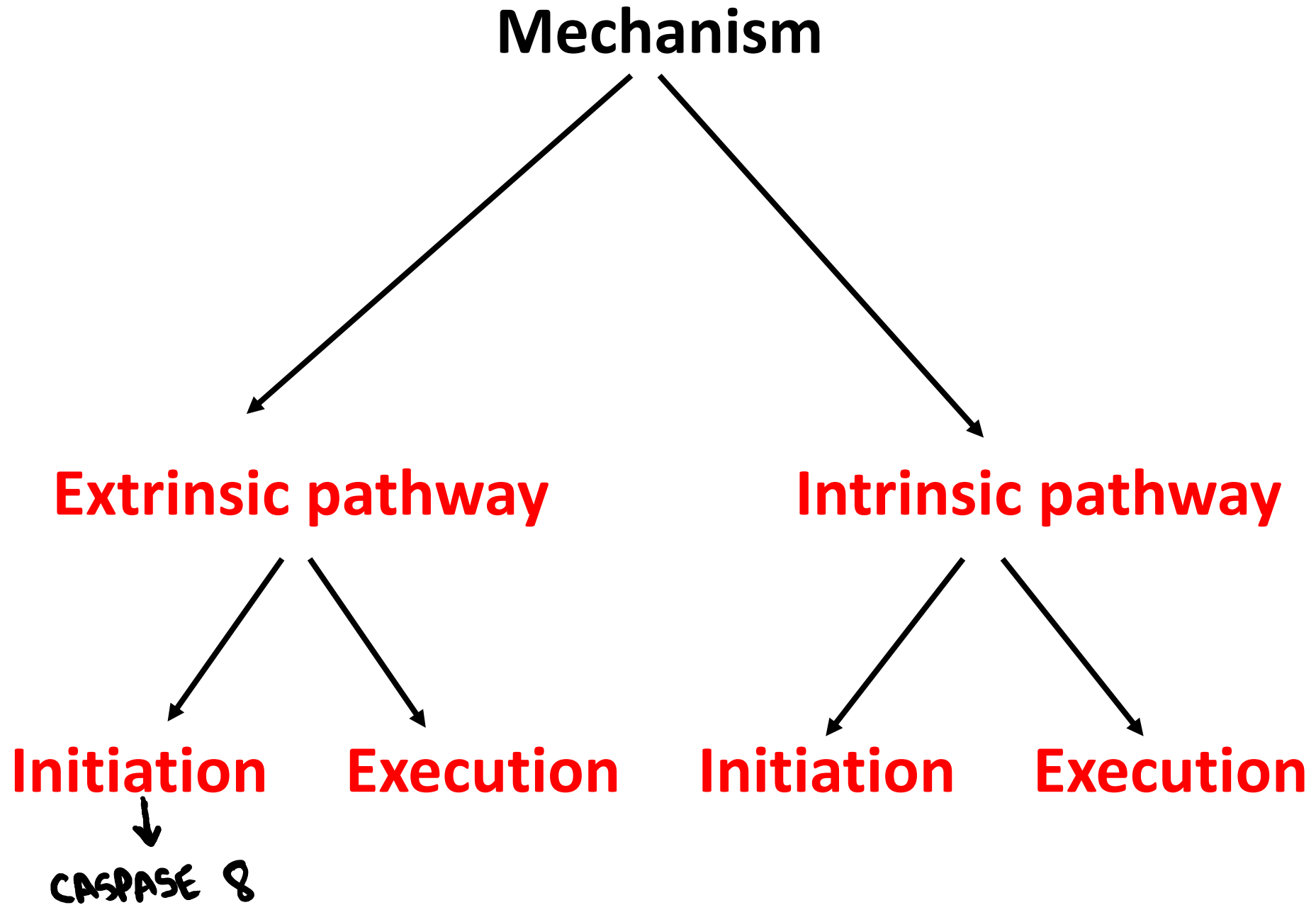
**Initiation**

**Execution**

**Initiation**

**Execution**

**CASPASE 8**





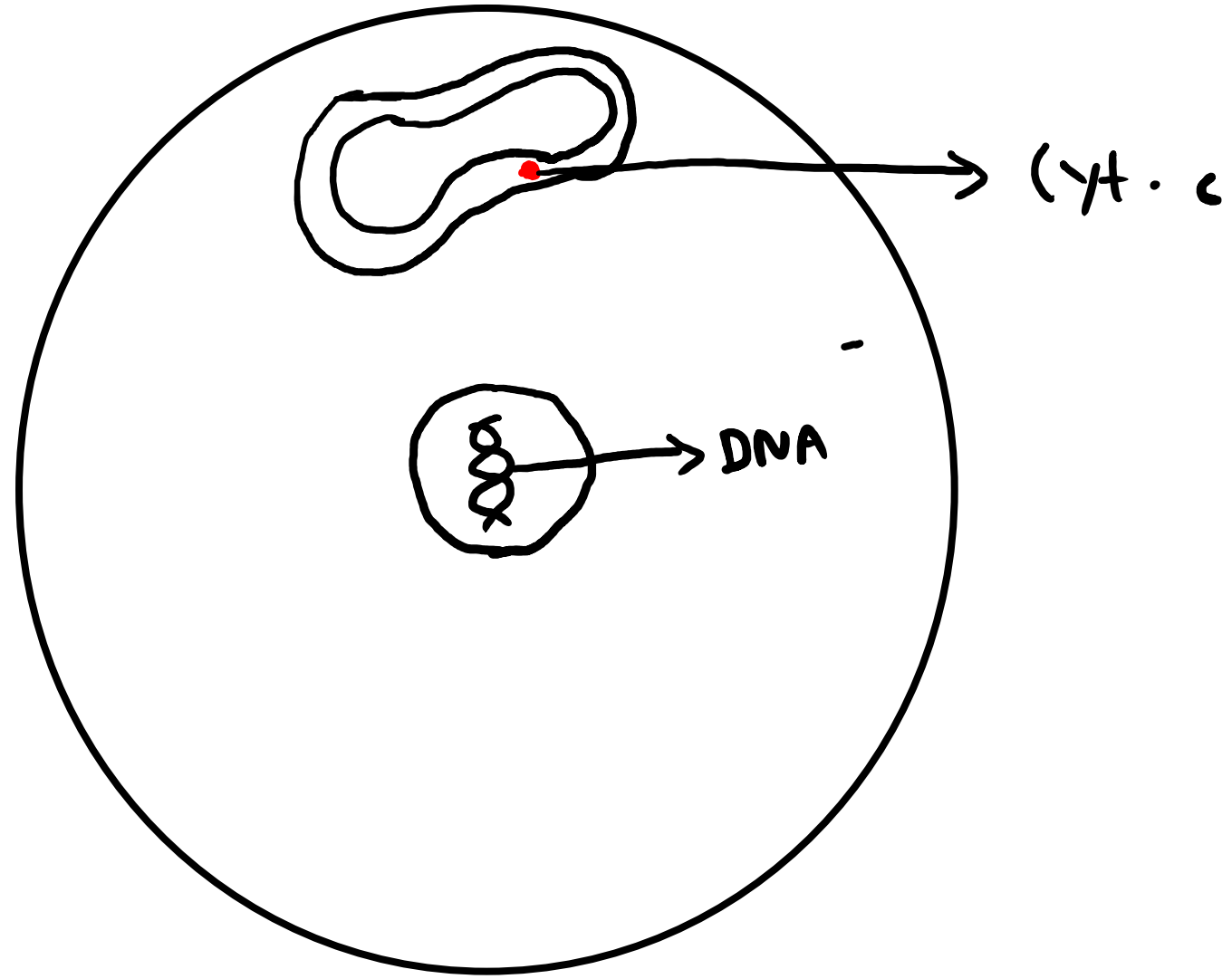
# **Intrinsic pathway → Initiation phase**

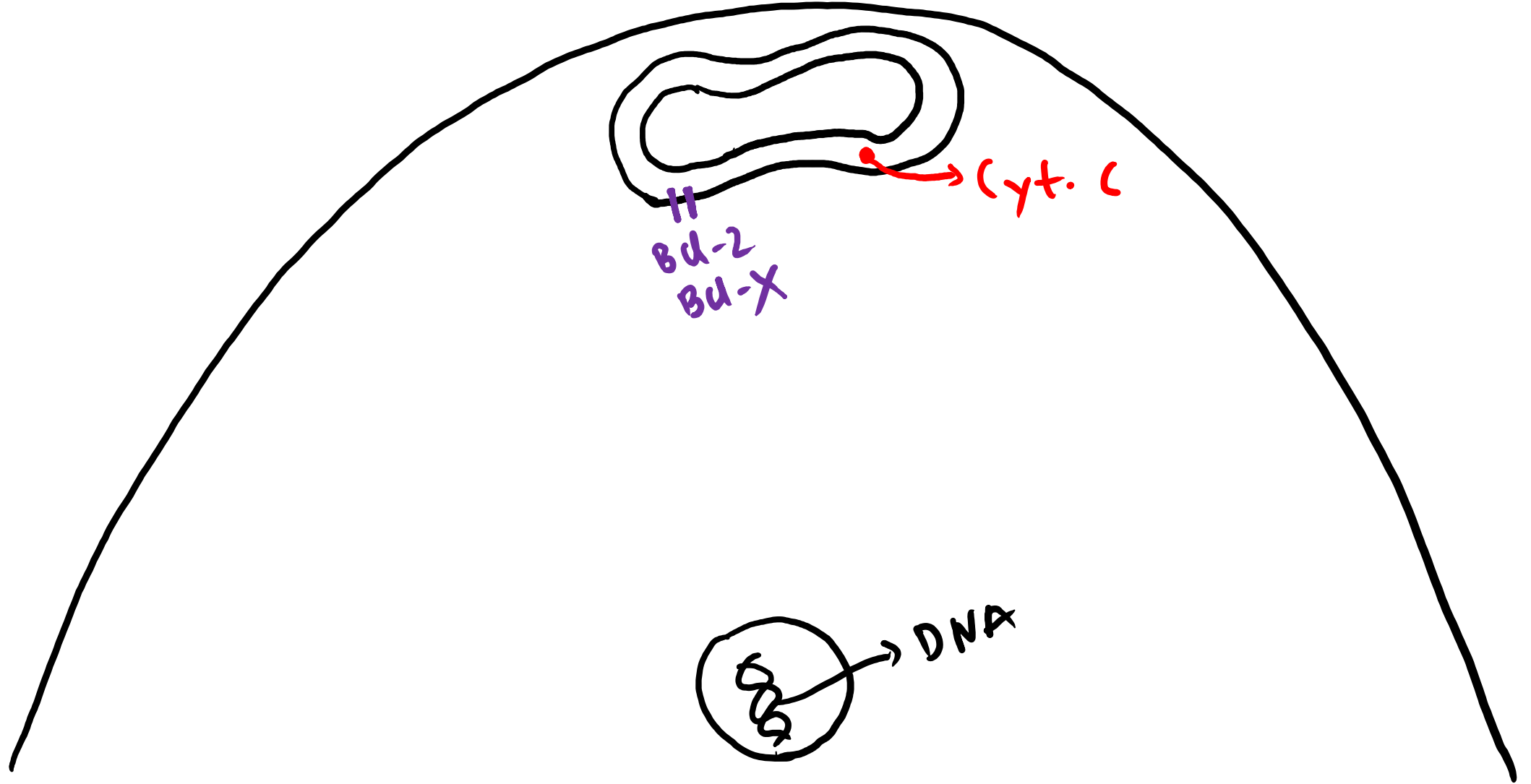
- The intrinsic signaling pathways that initiate apoptosis involve a diverse array of **non-receptor-mediated stimuli** that produce intracellular signals within the cell and are **mitochondrial-initiated events**

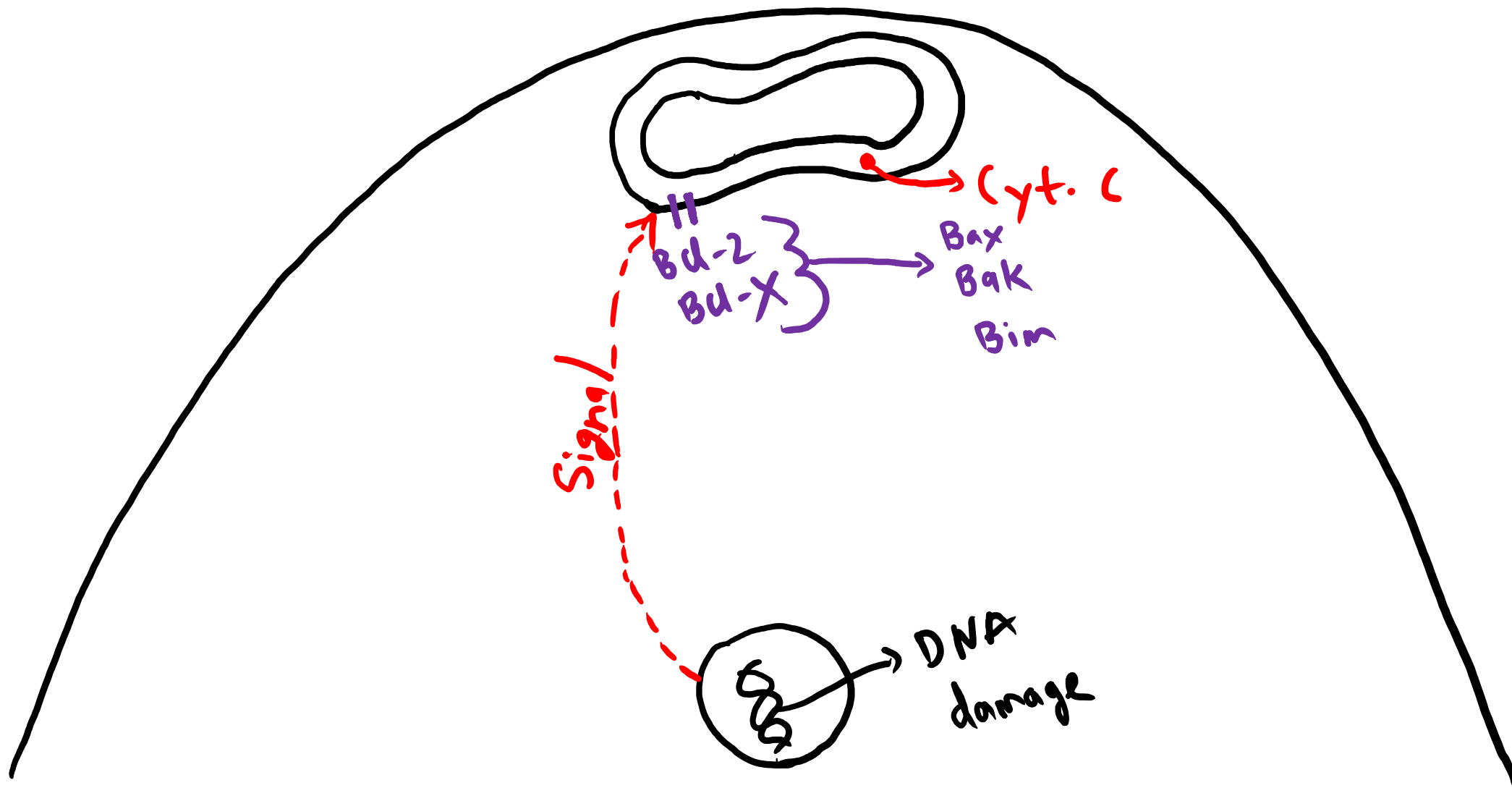
# Stimuli

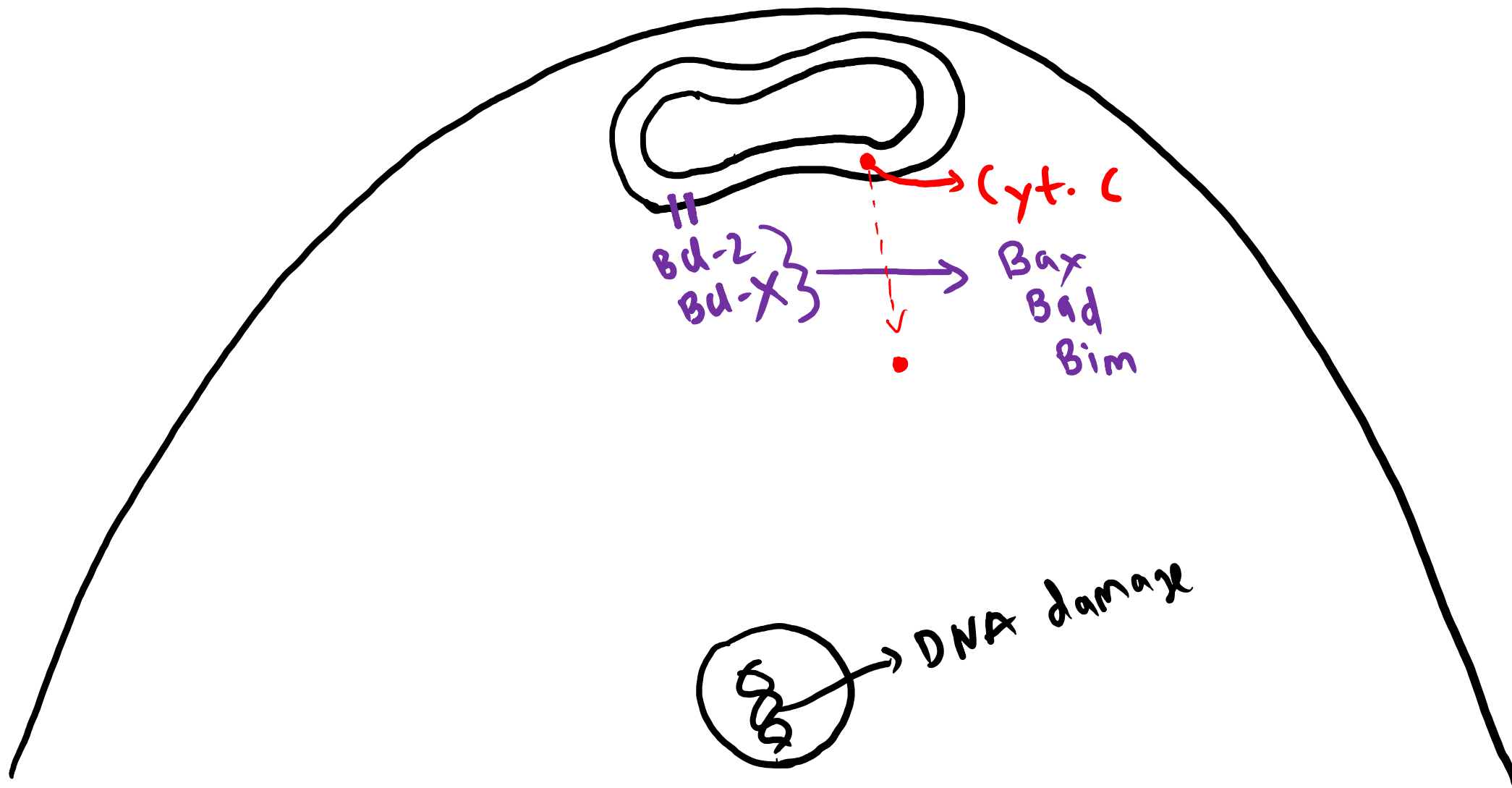
## DNA damage (beyond repair)

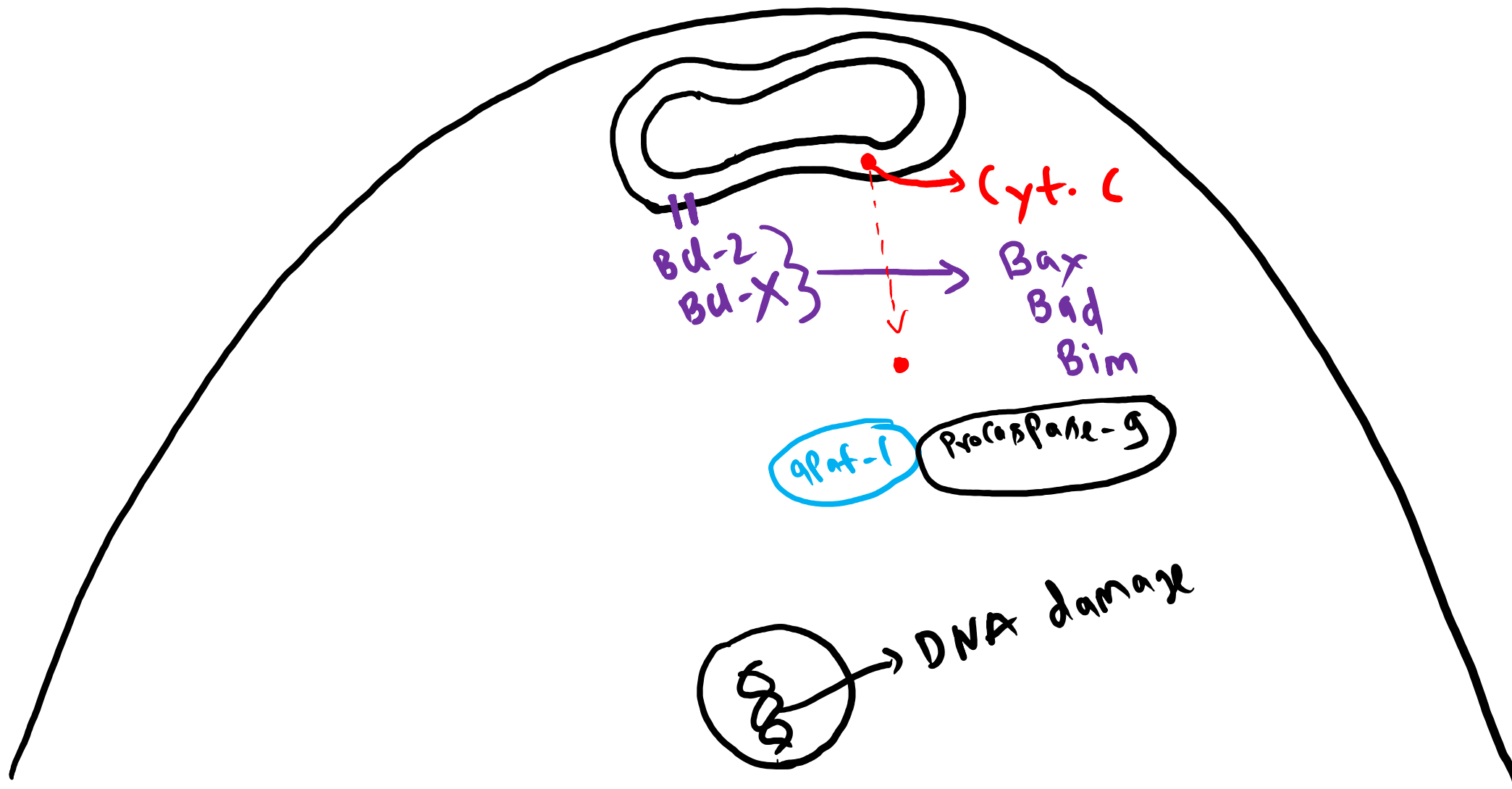
DNA damage can occur after exposure to agents like radiation and chemotherapy (genotoxic stress)

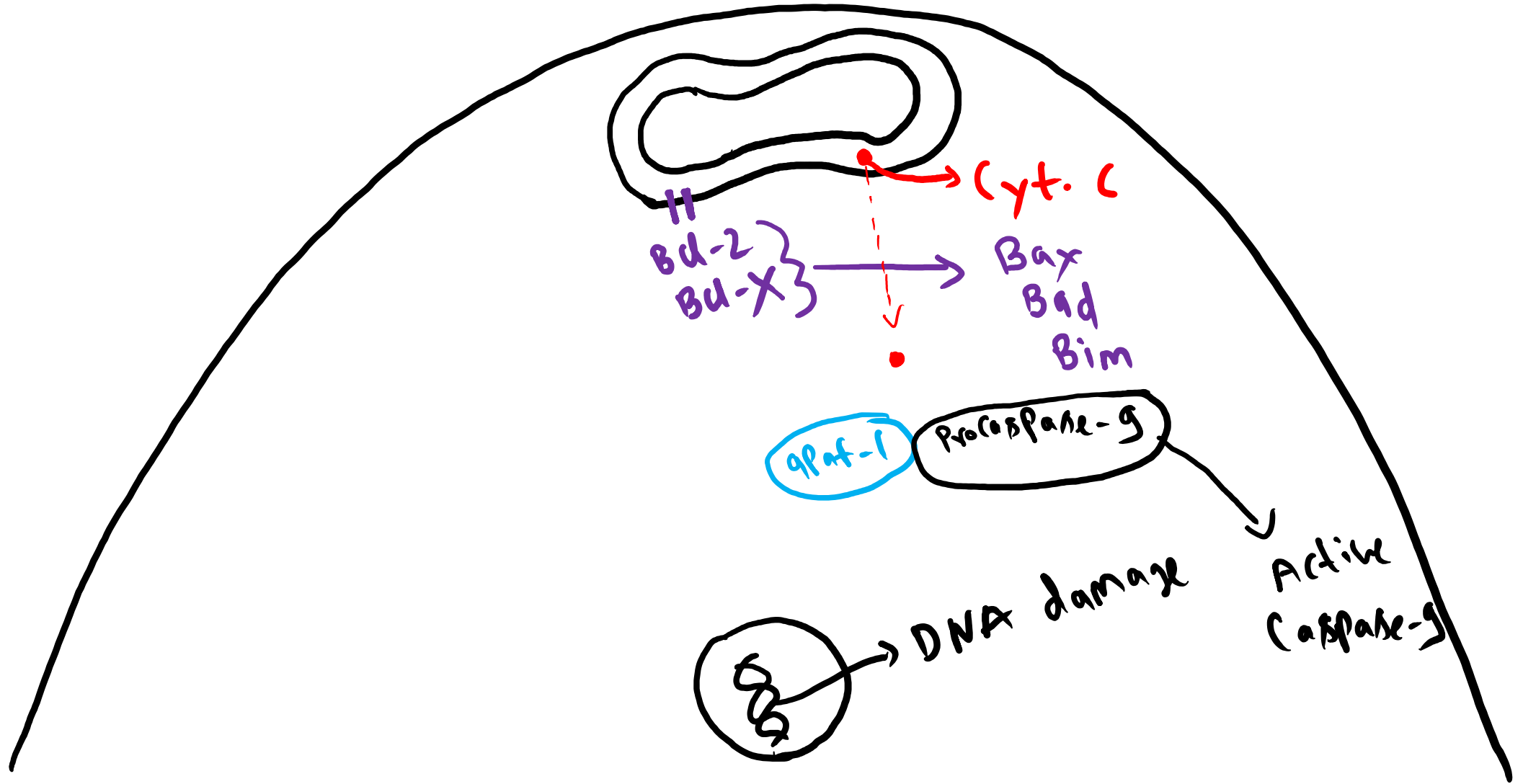




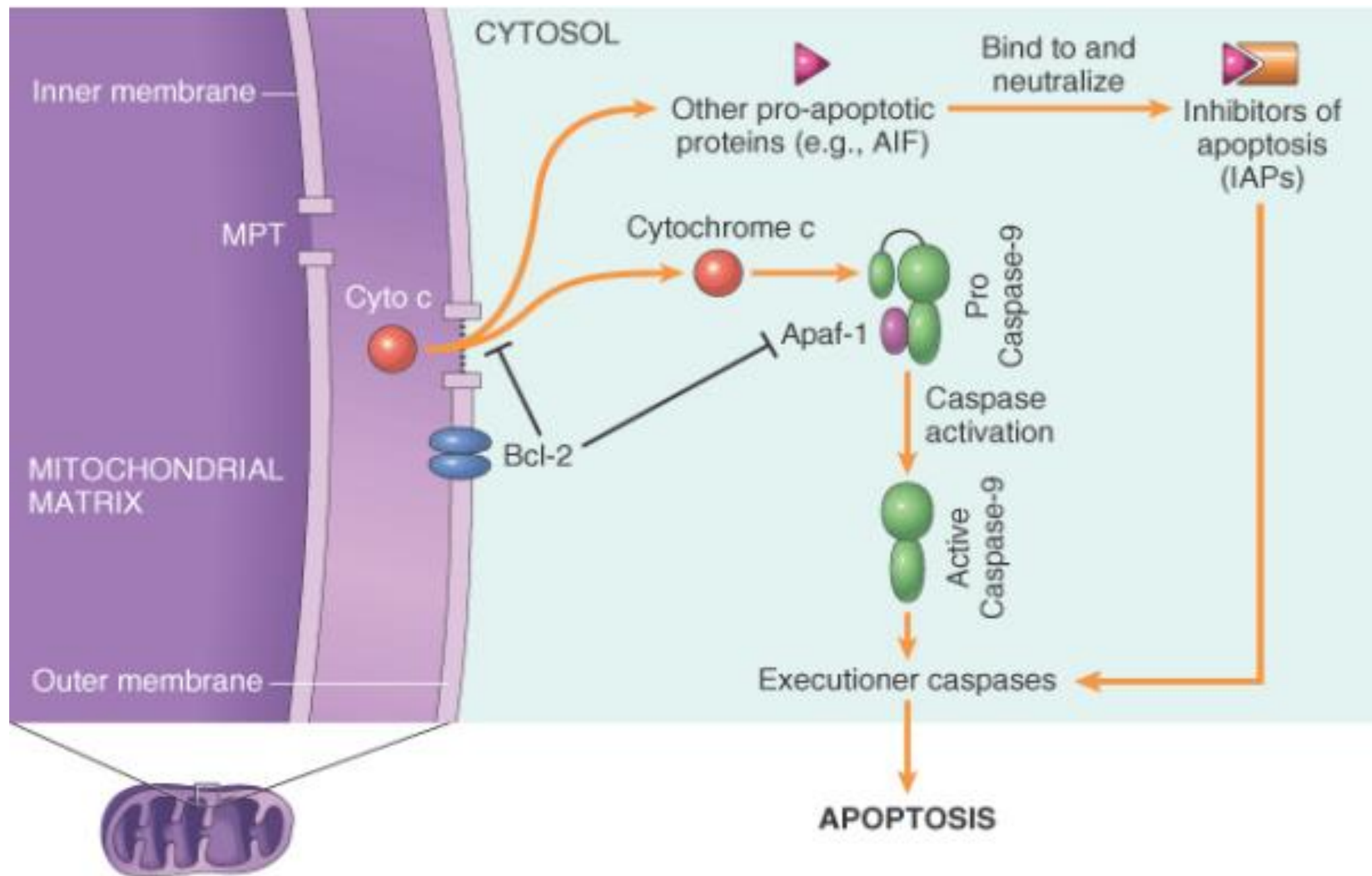












**Stimuli**



**Anti apoptotic molecules **Bcl-2 and Bcl-x** are lost**



**Replaced by pro-apoptotic molecules like **Bak, Bax, Bim****



**Increased mitochondrial permeability (MPT)**



**Release to cytochrome C into cytoplasm**



**Activates Apaf-1 along with procaspase-9**



**Activated caspase-9**

# **Antiapoptotic molecules**

1. BCL-2
2. BCL-X
3. Mcl-1
4. FLIP

# **Proapoptotic molecules**

1. Bax
2. Bim
3. Bad
4. Bak
5. P53 gene
6. Apaf-1
7. Cytochrome C

# REMEMBER

- **Mitochondria** are the most important organelles involved in initiation and regulation of apoptosis
- **Mitochondrial membrane permeabilization** is the hallmark of apoptosis

**Mechanism**

```
graph TD; Mechanism --> Extrinsic[Extrinsic pathway]; Mechanism --> Intrinsic[Intrinsic pathway]; Extrinsic --> Initiation1[Initiation]; Extrinsic --> Execution1[Execution]; Intrinsic --> Initiation2[Initiation]; Intrinsic --> Execution2[Execution];
```

**Extrinsic pathway**

**Intrinsic pathway**

**Initiation**

**Execution**

**Initiation**

**Execution**

# Mechanism

**Extrinsic pathway**

**Intrinsic pathway**

**Initiation**

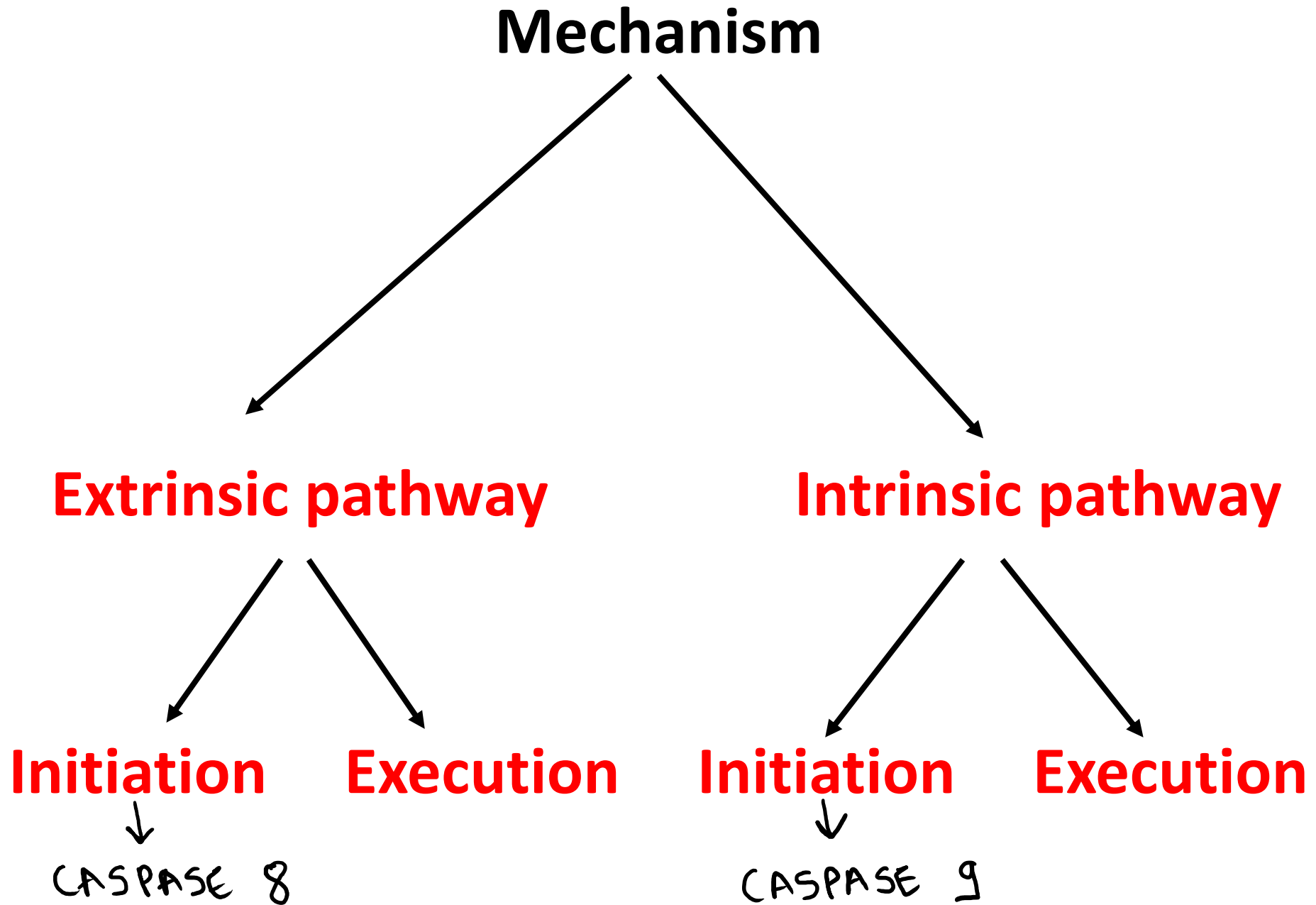
**Execution**

**Initiation**

**Execution**

CASPASE 8

CASPASE 9



# Execution phase

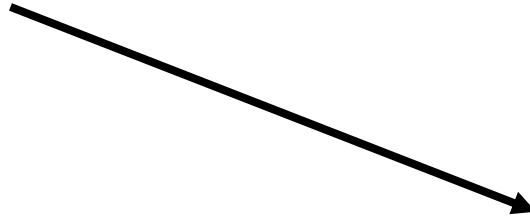
- It is a **convergence point** for both extrinsic and intrinsic pathways.



**Extrinsic pathway**



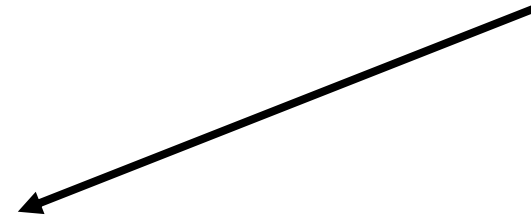
**Caspase 8**



**Intrinsic pathway**



**Caspase 9**



**Activates caspase 3 and 7**



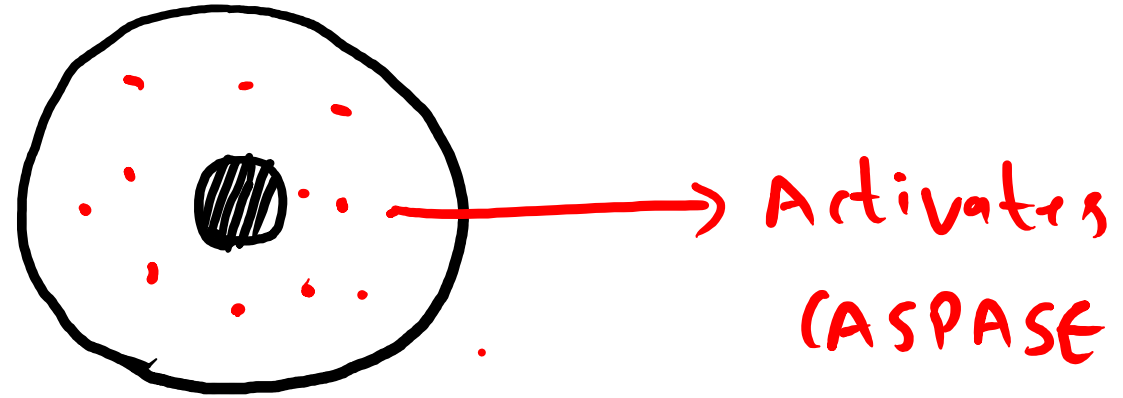
**Sequentially activates all other caspase**

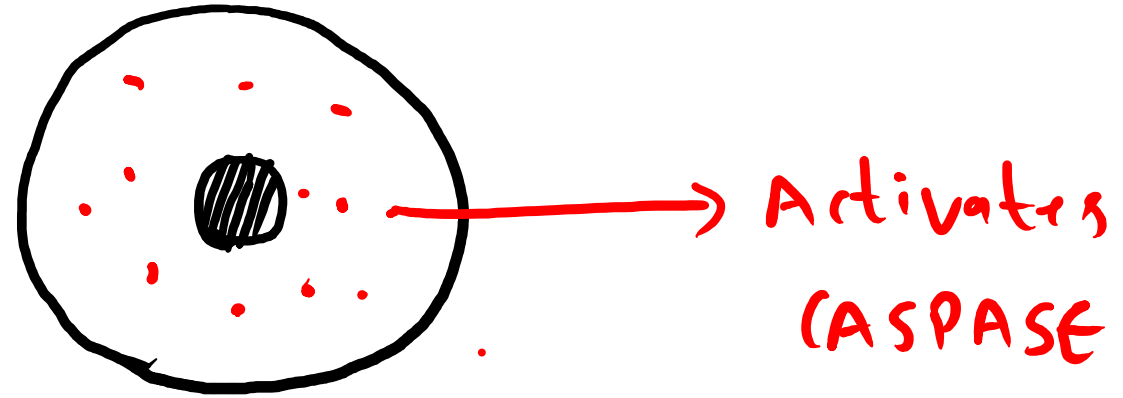


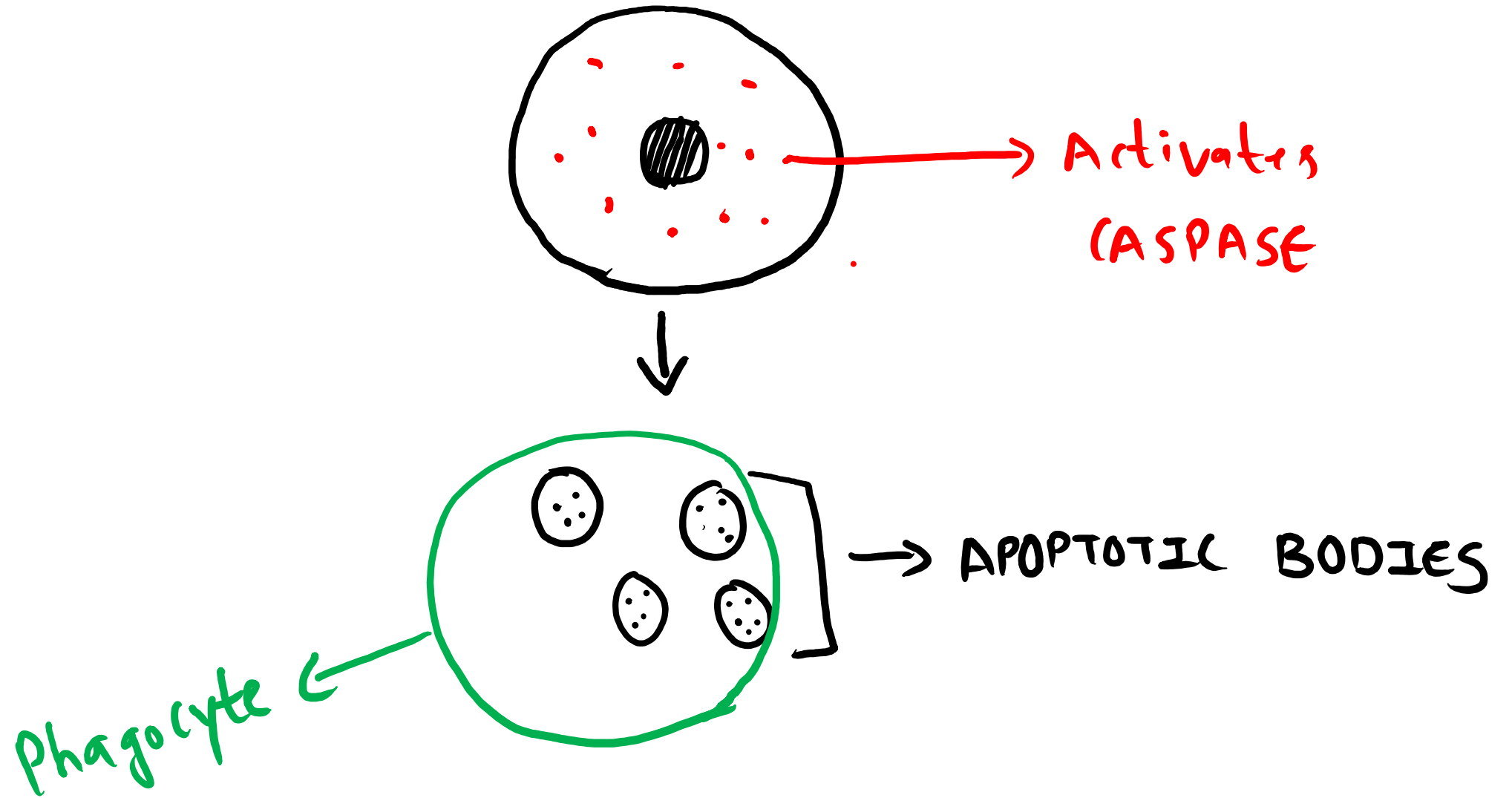
**Caspases cleave cytoskeletal and nuclear matrix proteins**



**Cell degenerate/ apoptotic bodies formed**



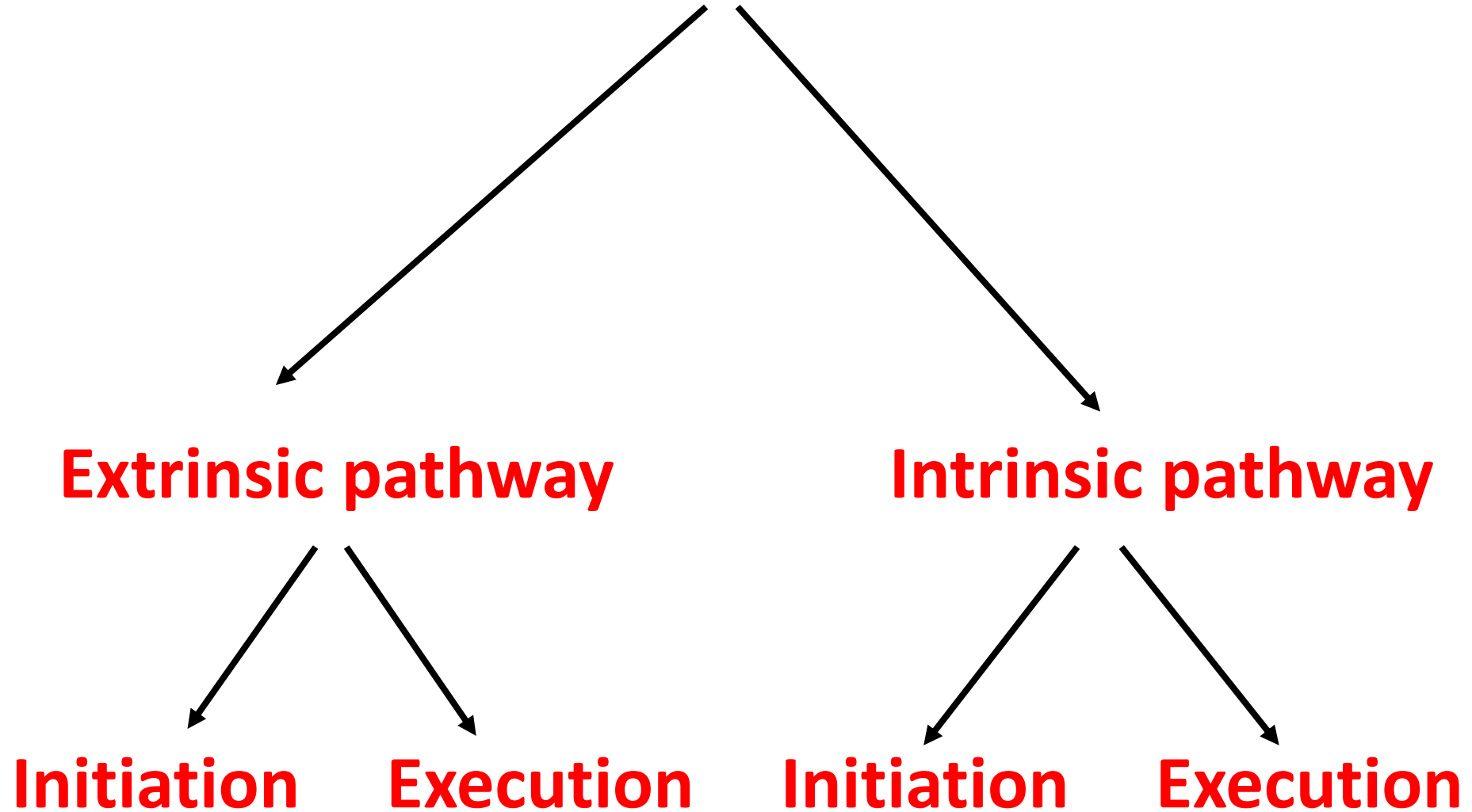




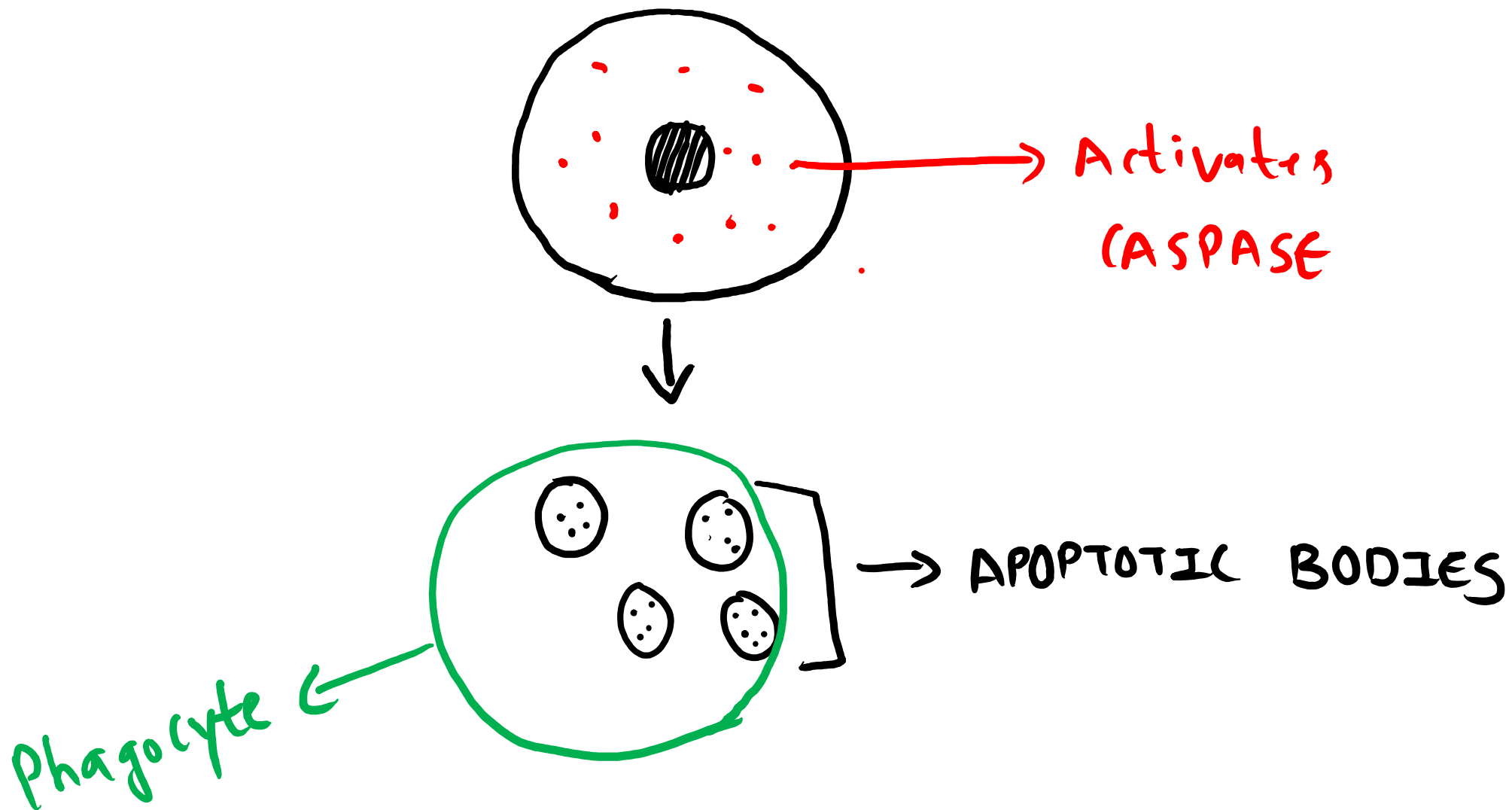
# REMEMBER

- Initiation Caspase → **CASPASE 8 and 9**
- Execution Caspase → **CASPASE 3 and 7**

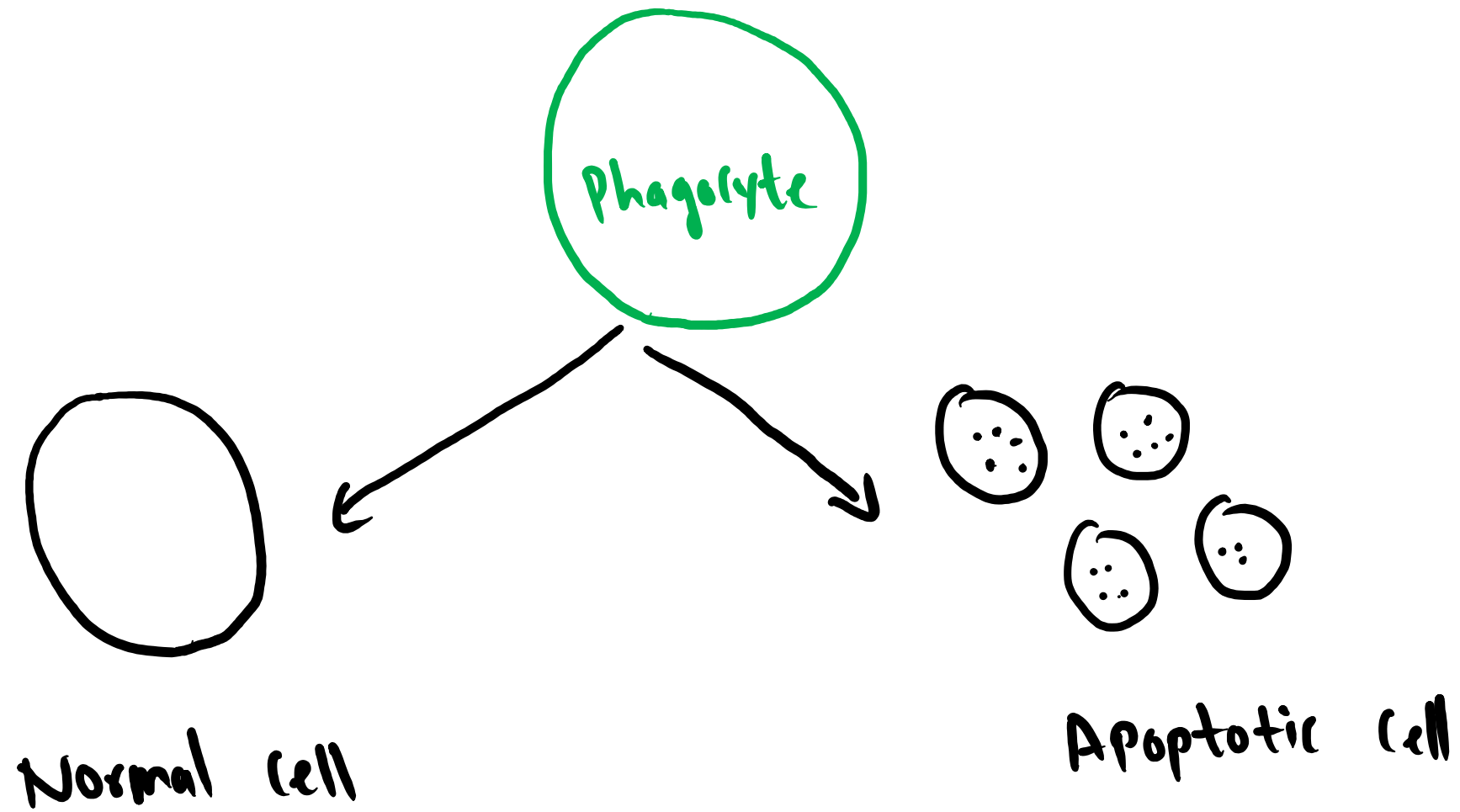
# Mechanism



# Phagocytosis







**Phosphatidylserine is a phospholipid present on inner surface membrane normally**



**During apoptosis**



**Flipped to outer surface**

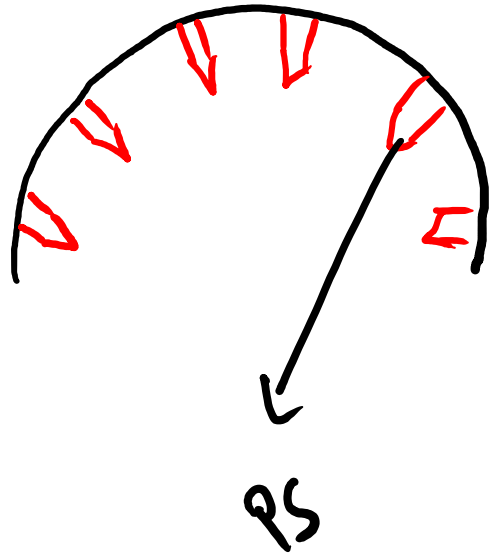


**Externalization of phosphatidylserine causes its tagging**

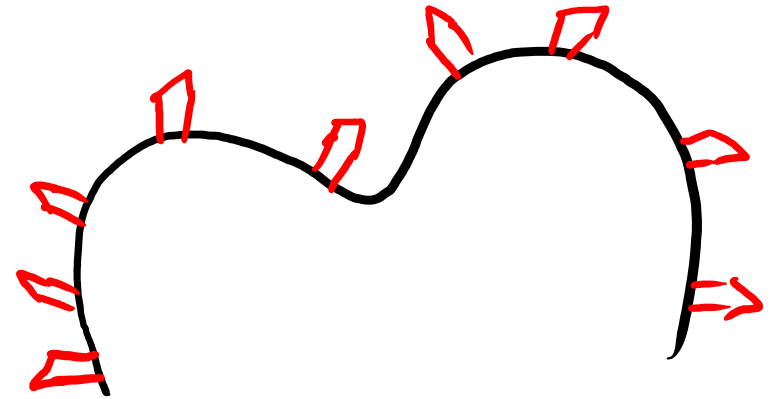


**Phagocytes engulf it**

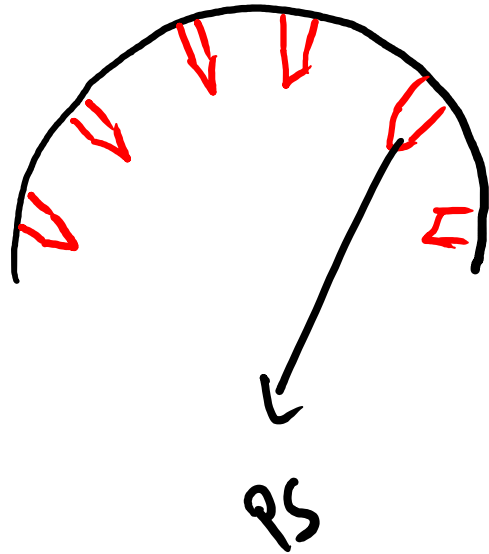
Normally



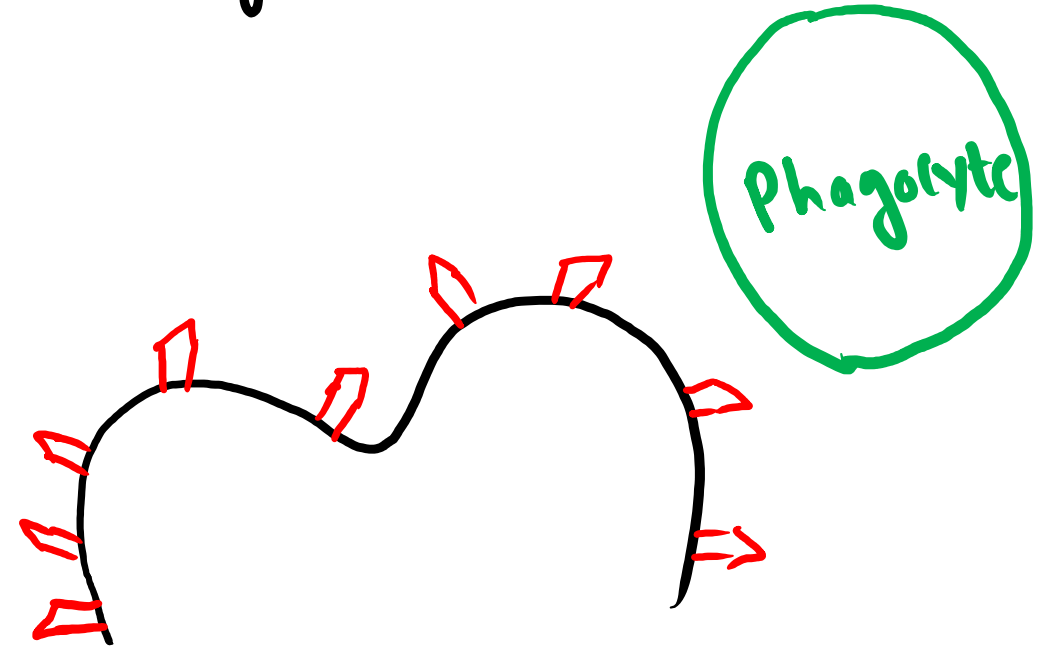
During apoptosis



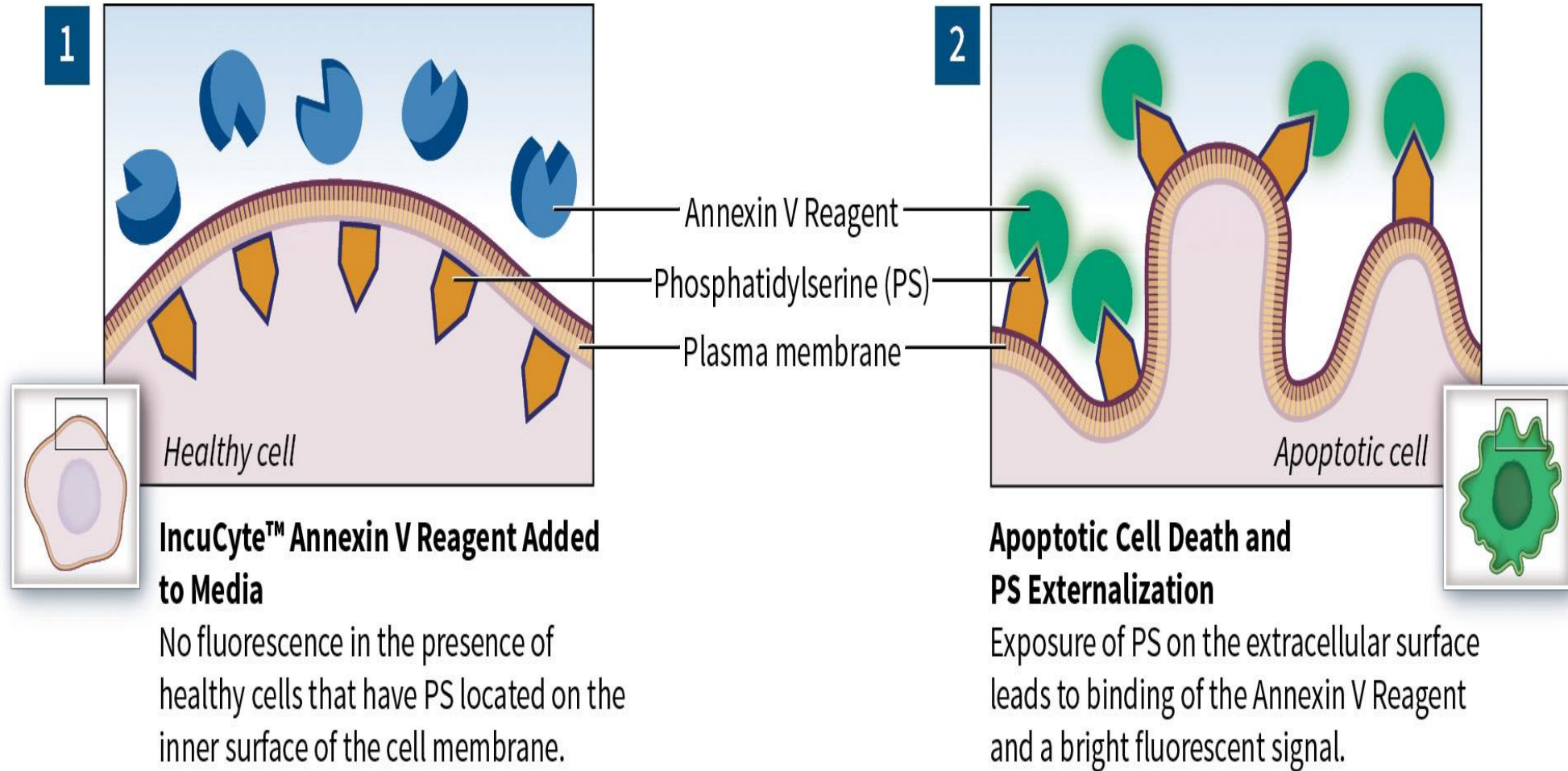
Normally



During apoptosis



## Annexin V overview schematic



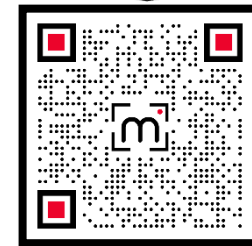
These alterations permit the early recognition of apoptotic cells by macrophages



Phagocytosis without the release of proinflammatory cellular components.

- The process of apoptotic cells is so efficient that dead cells disappear without leaving a trace and **inflammation is virtually absent.**

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Telegram group discussion*



- **Essential feature is immediate, specific and non-inflammatory nature of phagocytosis**



# POLLS

*Scan or Click to watch  
Cell Adaptation & Injury*



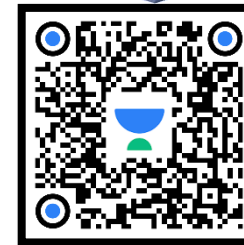
*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*



**CD 95 is a marker of -**

- a) Intrinsic pathway of apoptosis**
- b) Extrinsic pathway of apoptosis**
- c) Monocyte**
- d) Leucocyte**

**CD 95 is a marker of -**

- a) Intrinsic pathway of apoptosis
- b) Extrinsic pathway of apoptosis**
- c) Monocyte
- d) Leucocyte

# **In apoptosis, cytochrome C acts through**

- a) Apaf 1**
- b) Bcl-2**
- c) FADD**
- d) TNF**

# **In apoptosis, cytochrome C acts through**

**a) Apaf 1**

**b) Bcl-2**

**c) FADD**

**d) TNF**

**The following is an antiapoptotic gene -**

- a) Bax
- b) Bad
- c) Bcl-X
- d) Bim

# **The following is an antiapoptotic gene -**

- a) Bax
- b) Bad
- **c) Bcl-X**
- d) Bim

# **OVERVIEW**

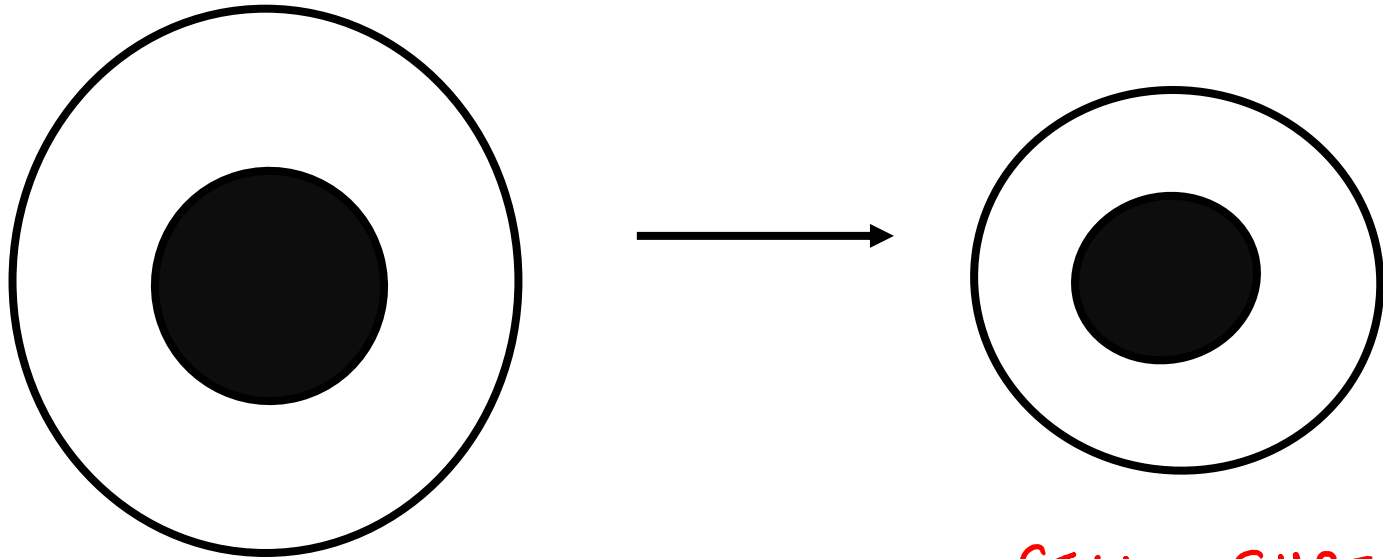
- **Definition**
- **Types**
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- **Diagnosis of Apoptosis**
- **Differences from necrosis**



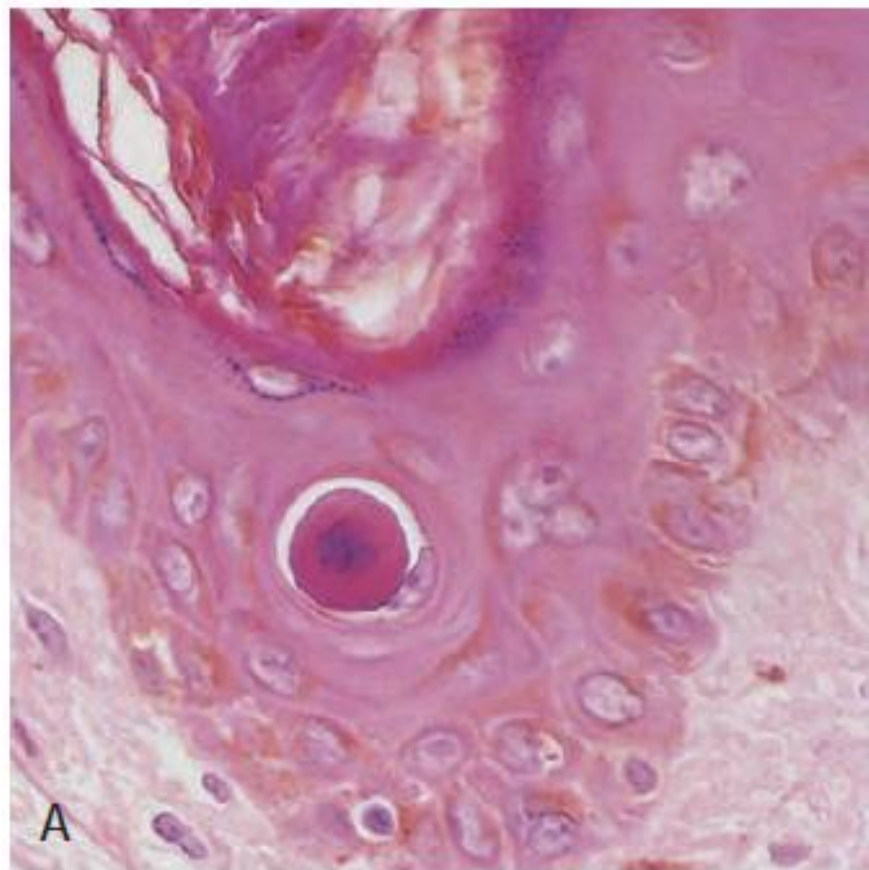
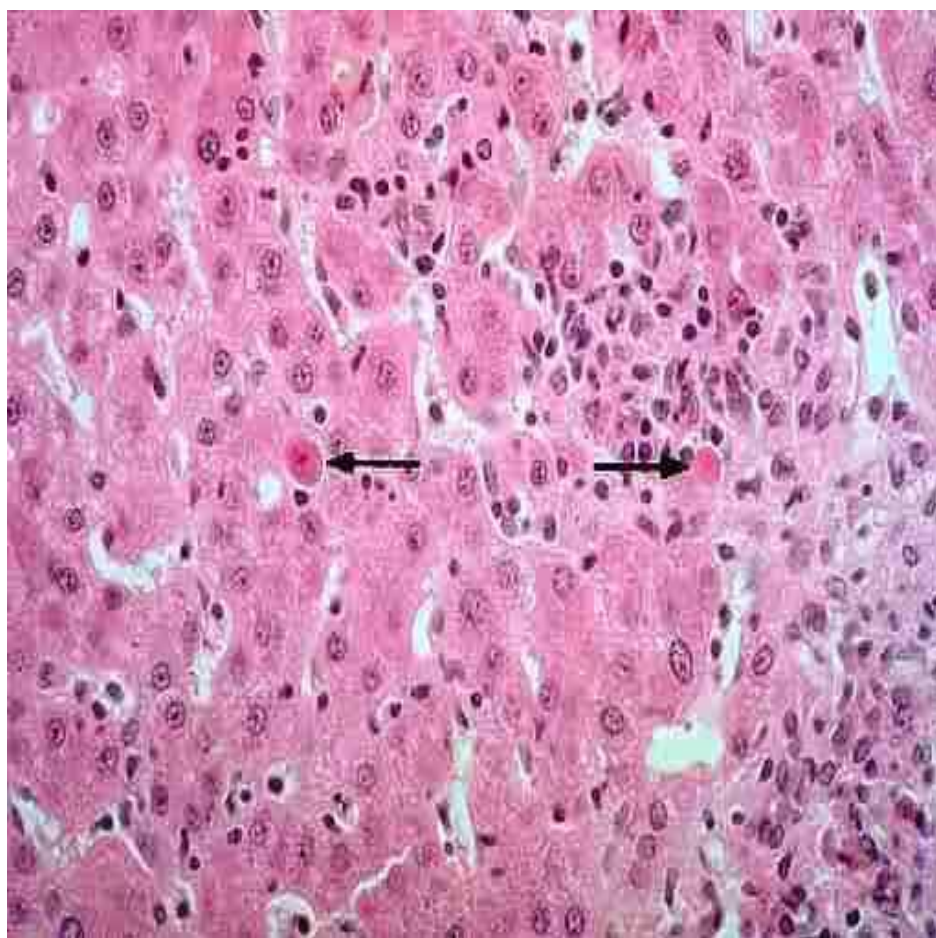
# **Morphological changes in apoptosis**

**1. Cellular shrinkage** is **earliest change**

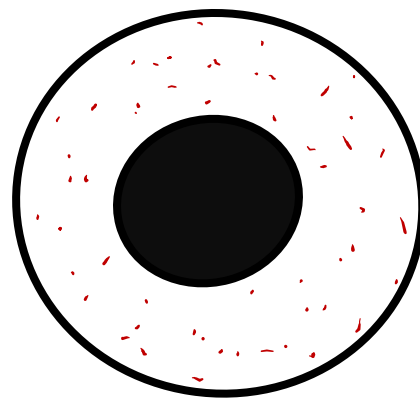
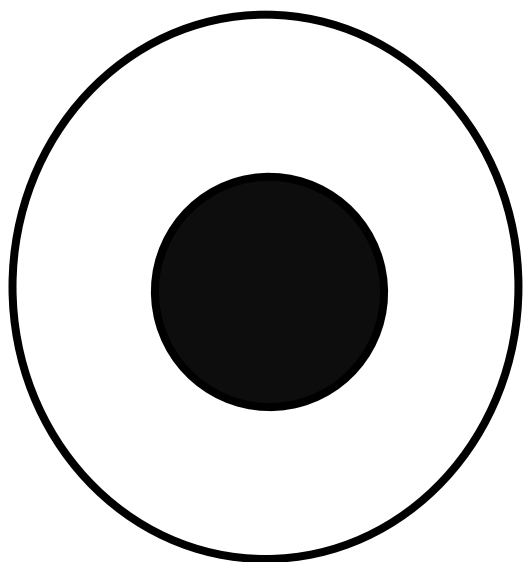
- It is due to damage to cytoskeletal proteins.



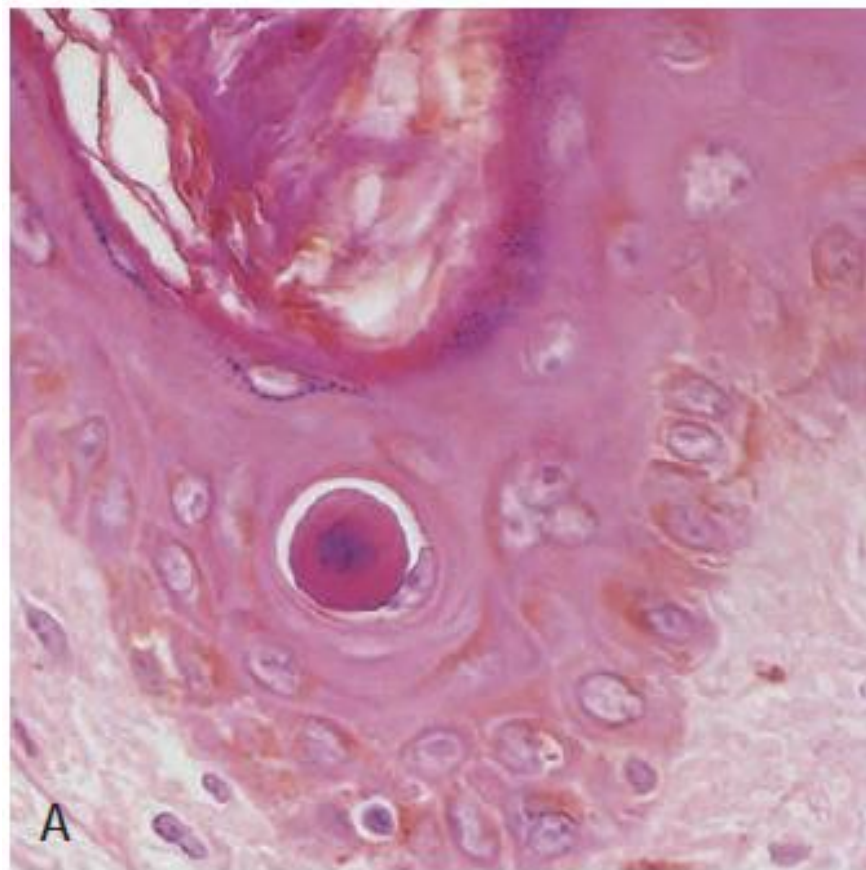
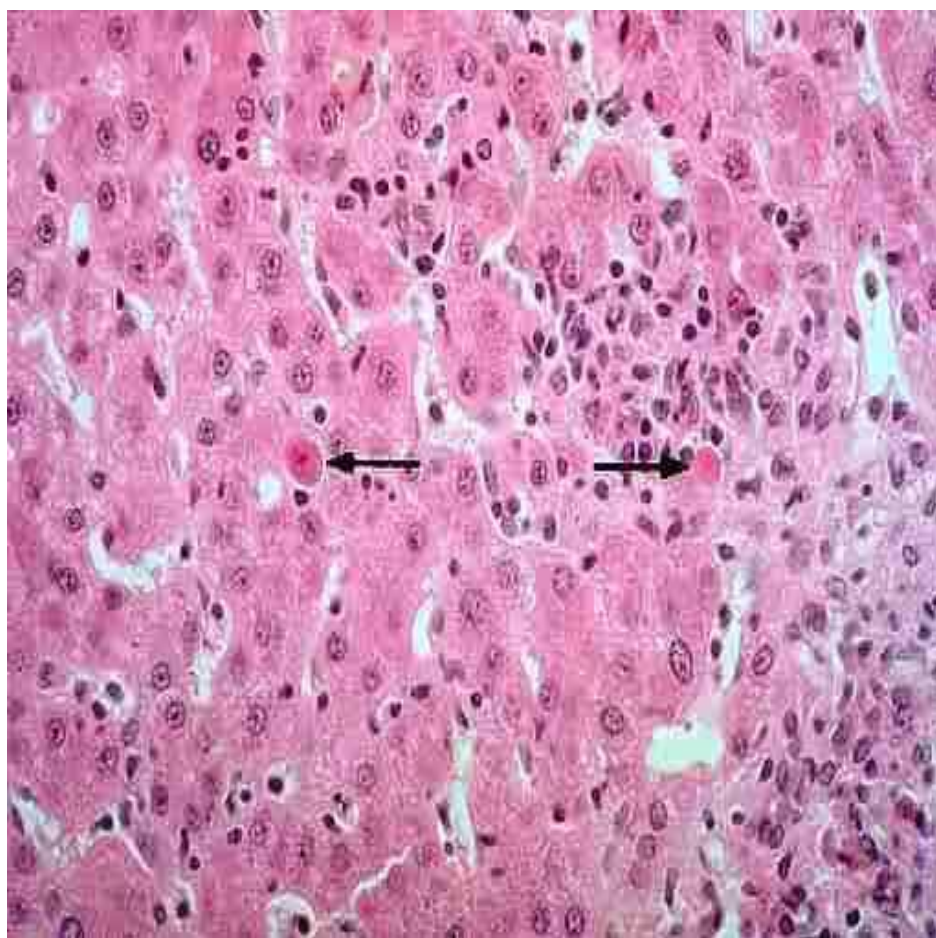
CELL SHRINKAGE



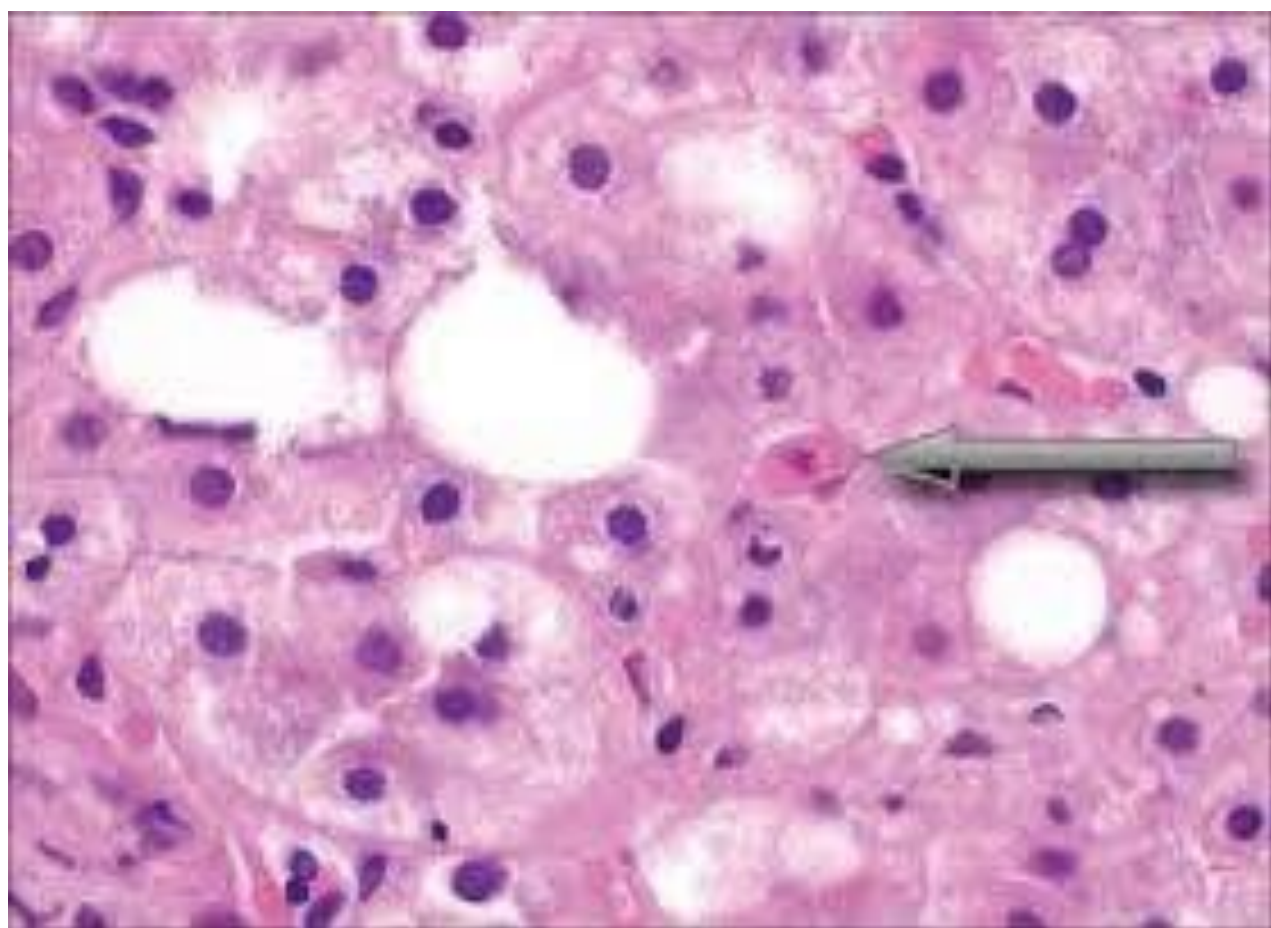
**2. Cellular organelles are tightly packed** thus imparting intense **eosinophilic** color to cytoplasm



EOSINOPHILIA



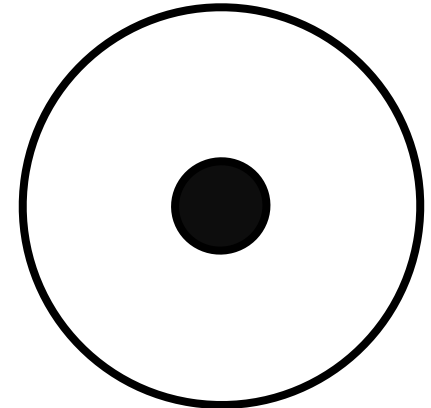
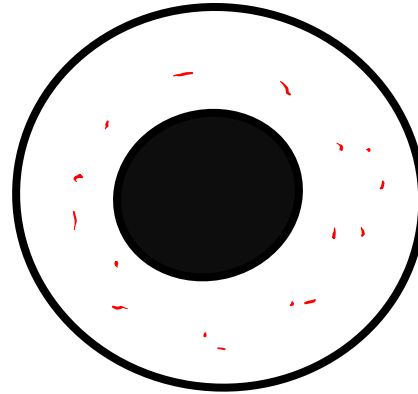
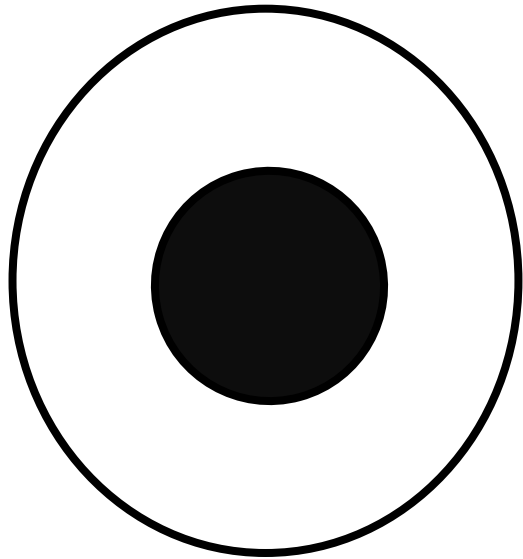




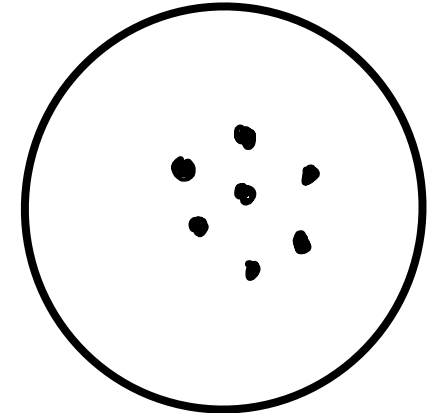


### 3. Nuclear changes

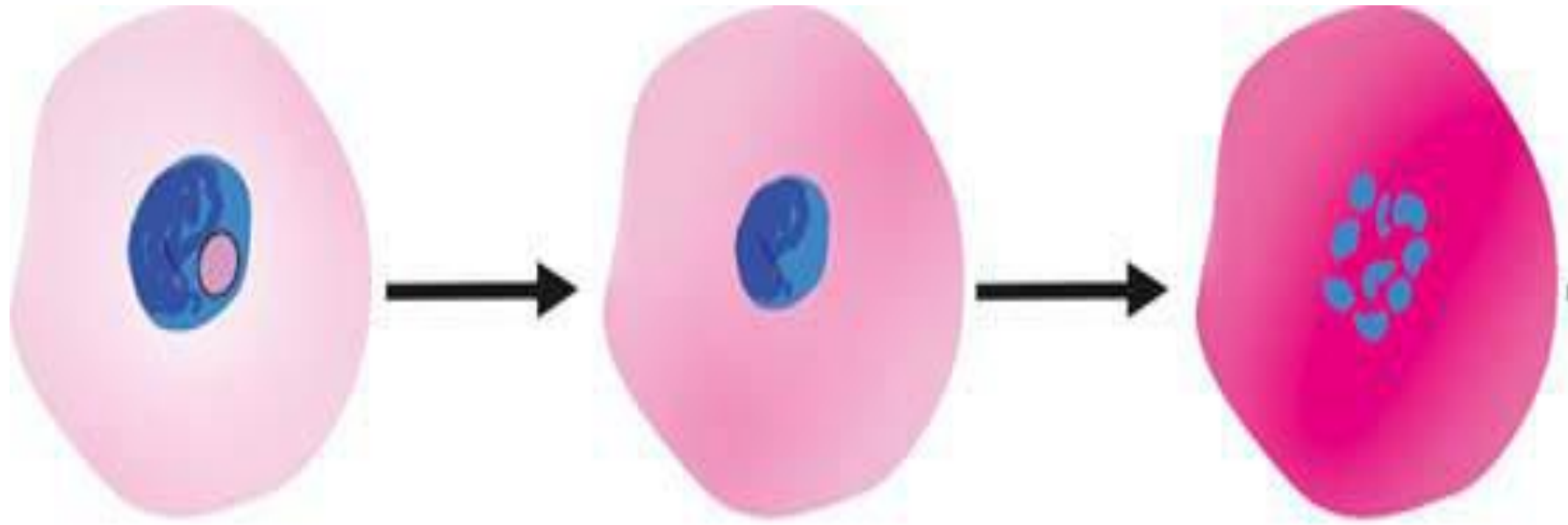
- **Pyknosis** ie. Chromatin condensation or nuclear compaction
- **Karyorrhexis** ie. nuclear fragmentation. It is due to activity of endonuclease and caspases
- It is the **most characteristic feature**



PYKNOSIS



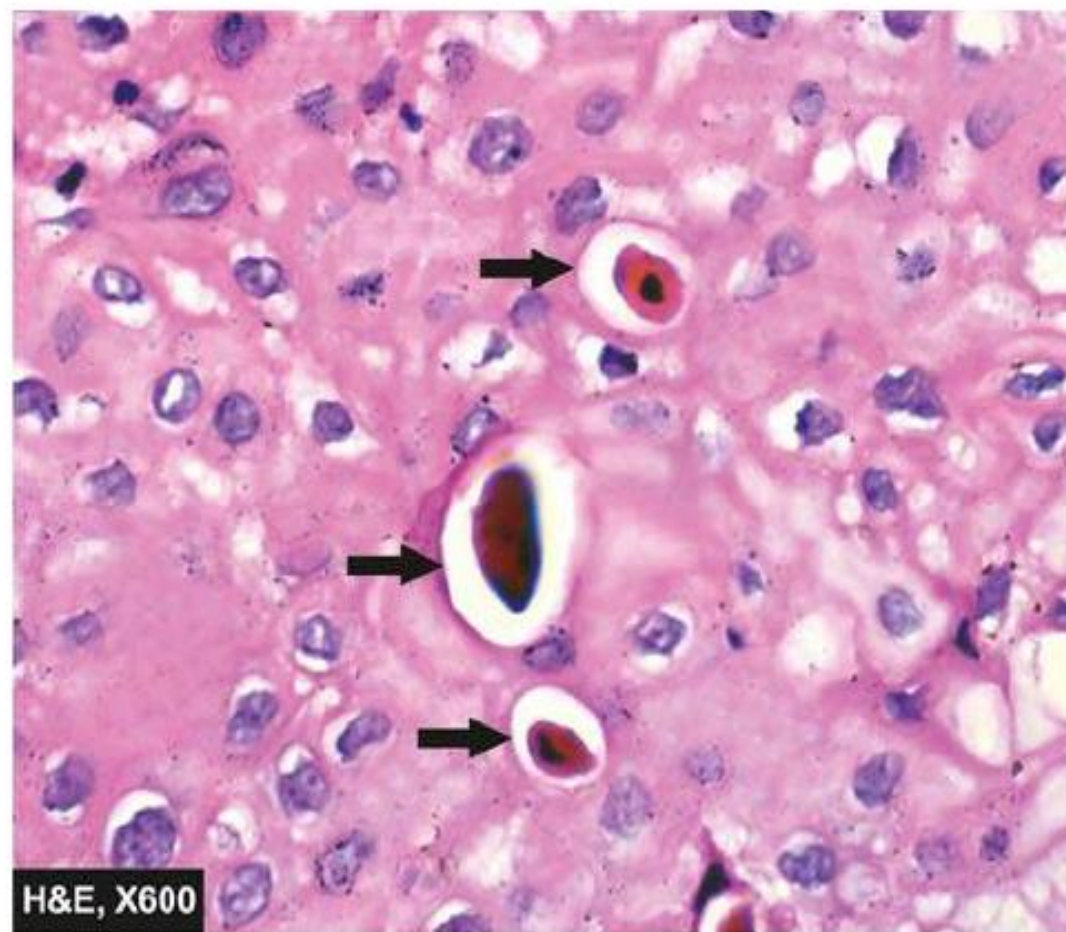
KARYORRHEXIS

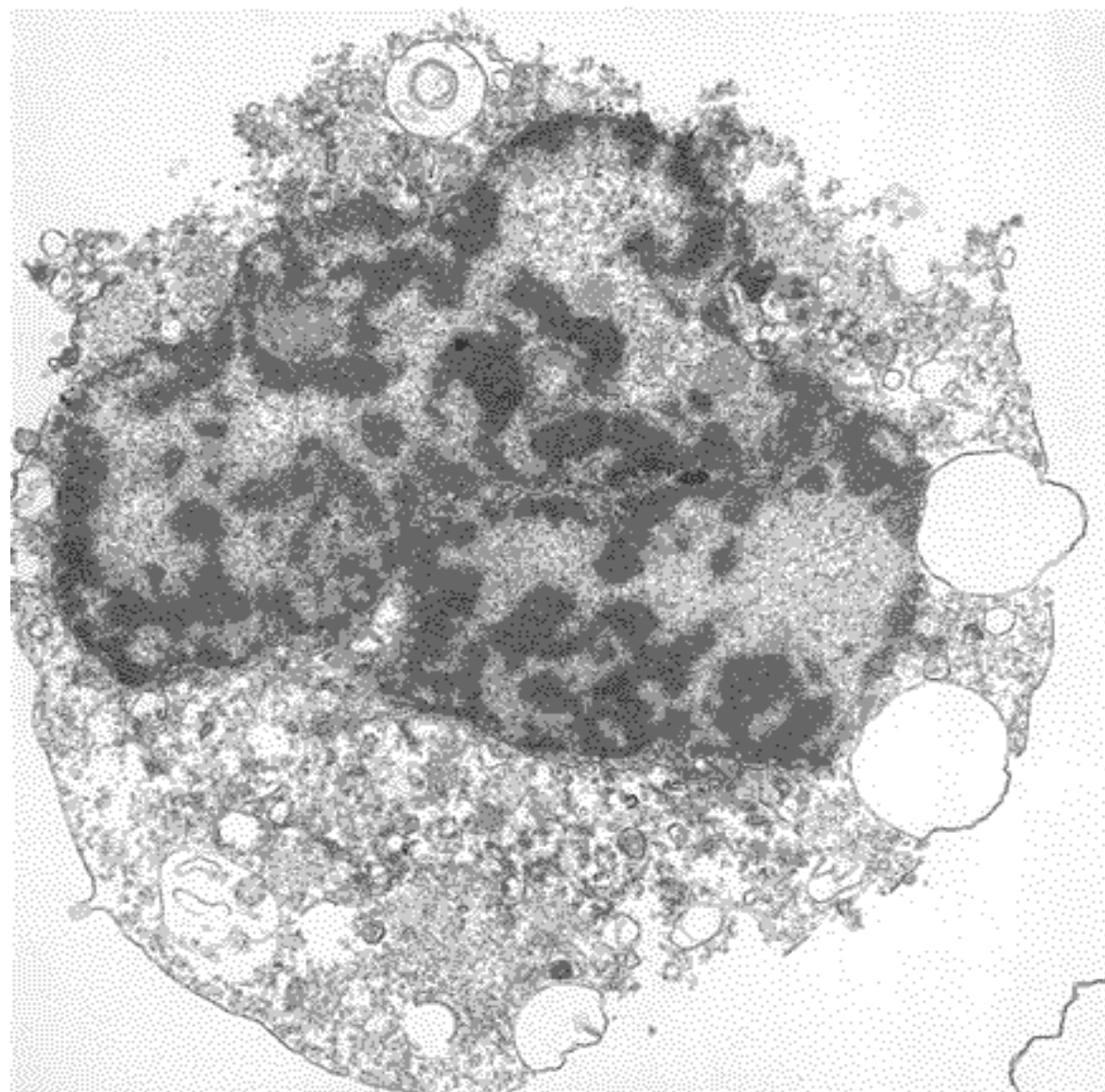
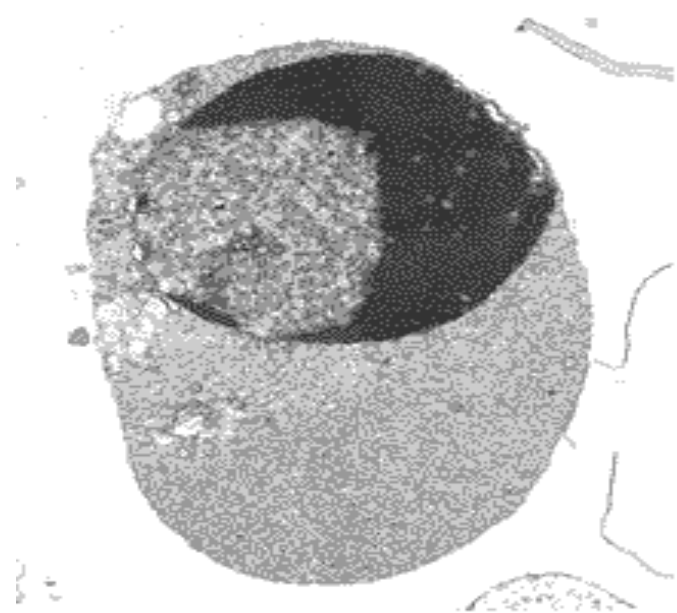


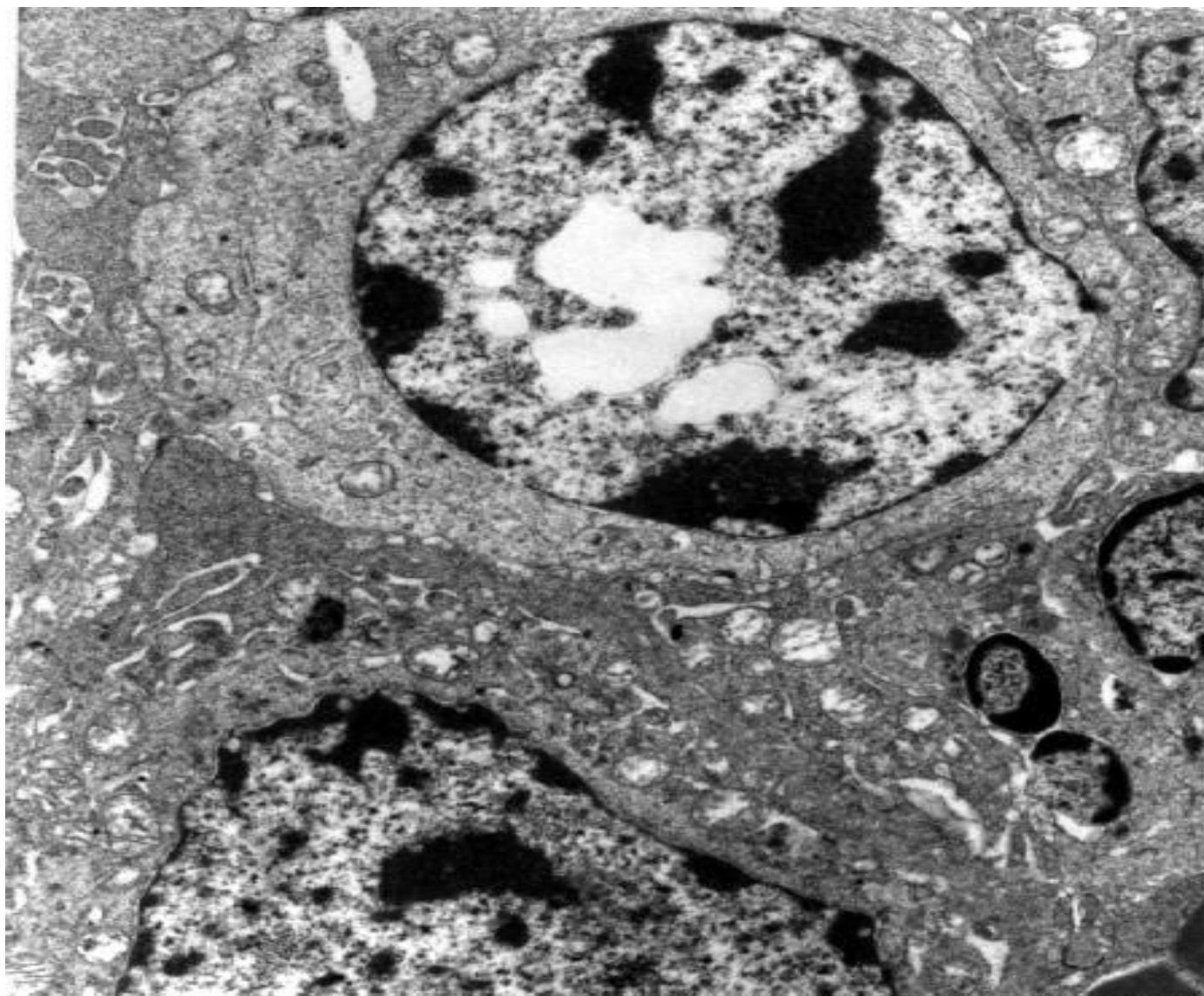
A, Normal cell

B, Pyknosis

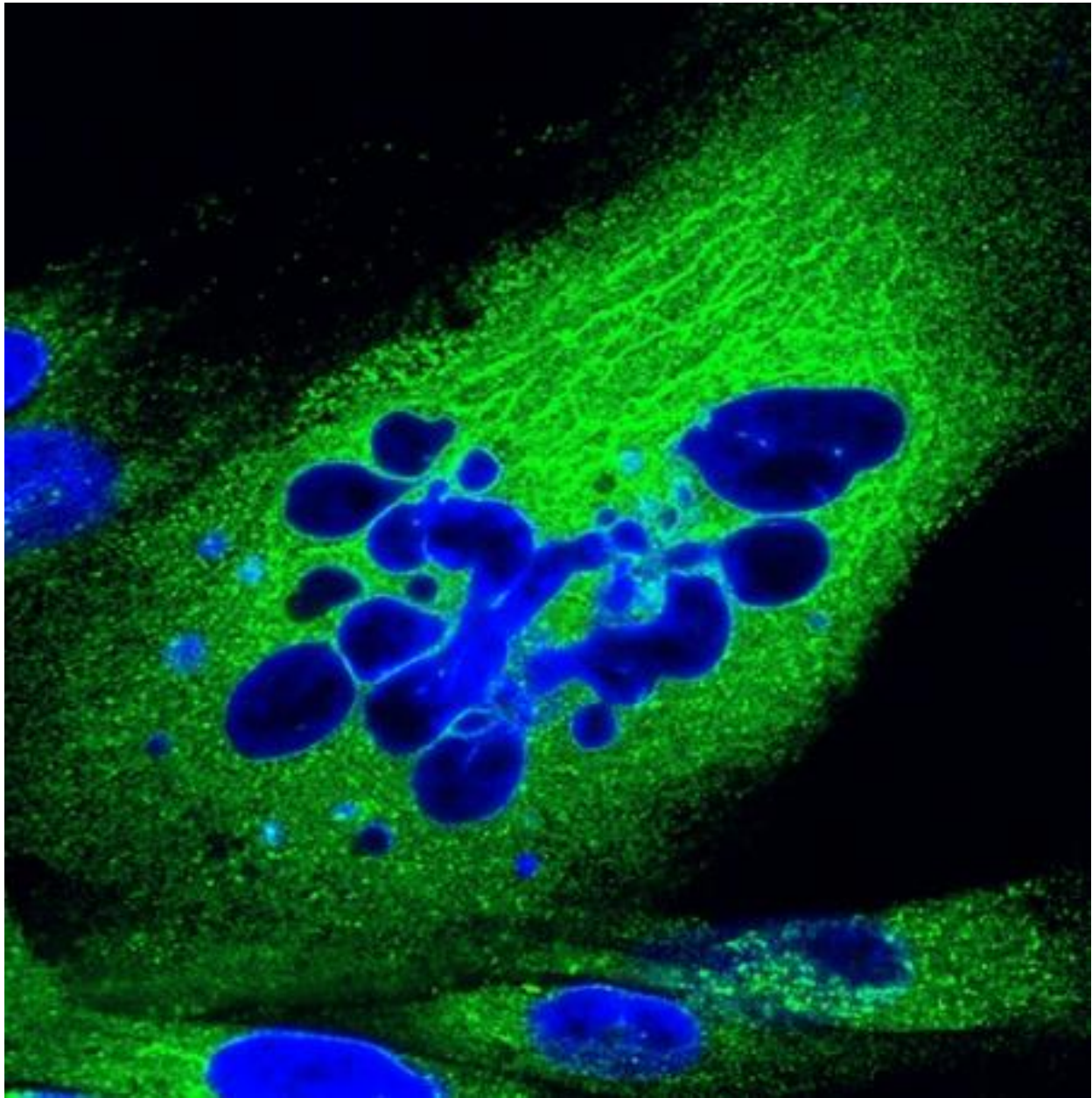
C, Karyorrhexis







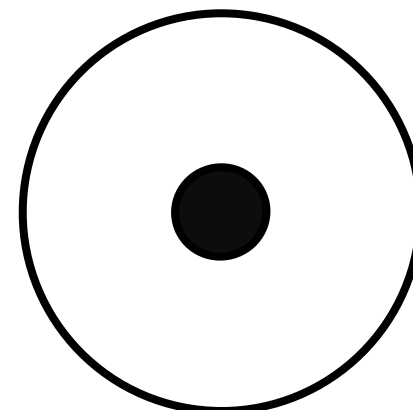
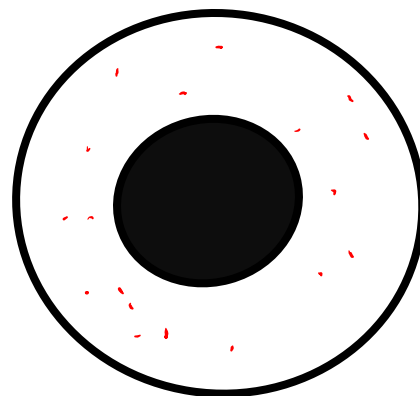
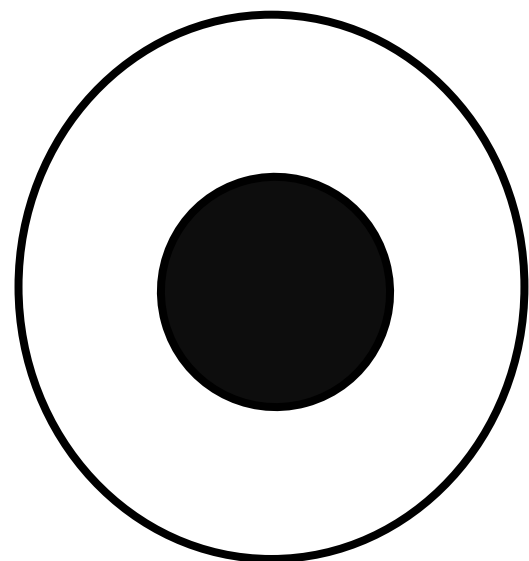




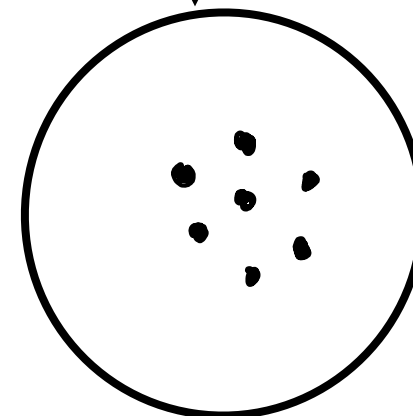
4. Cytoplasmic membrane shows **multiple surface blebs.**

- It is the **end stage** of apoptosis.
- **Cell membrane intact** thus **preventing leaking out** of cellular contents.

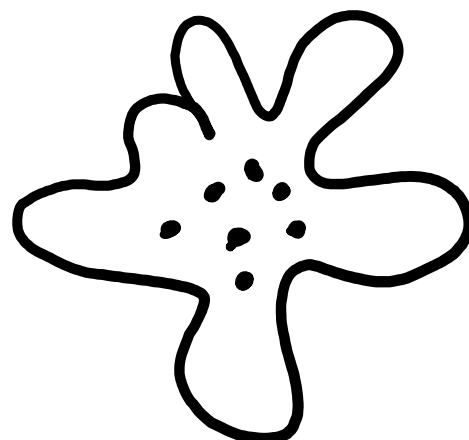




PYKNOSIS

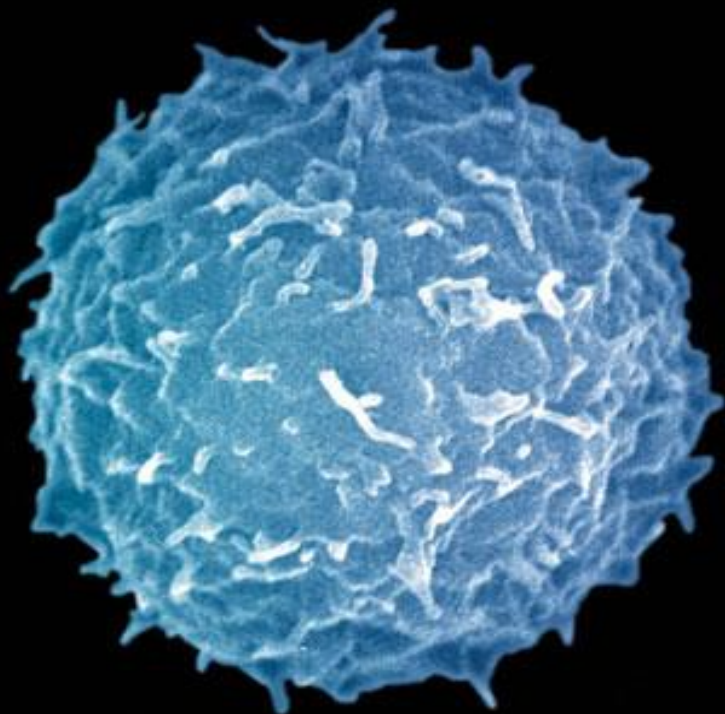


KARYORRHEXIS

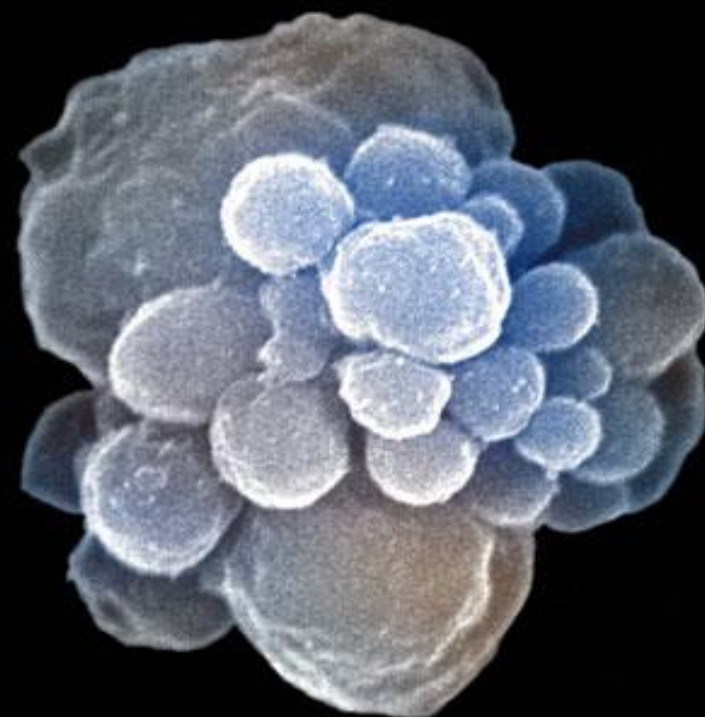


BLEBS

**normal WBC**

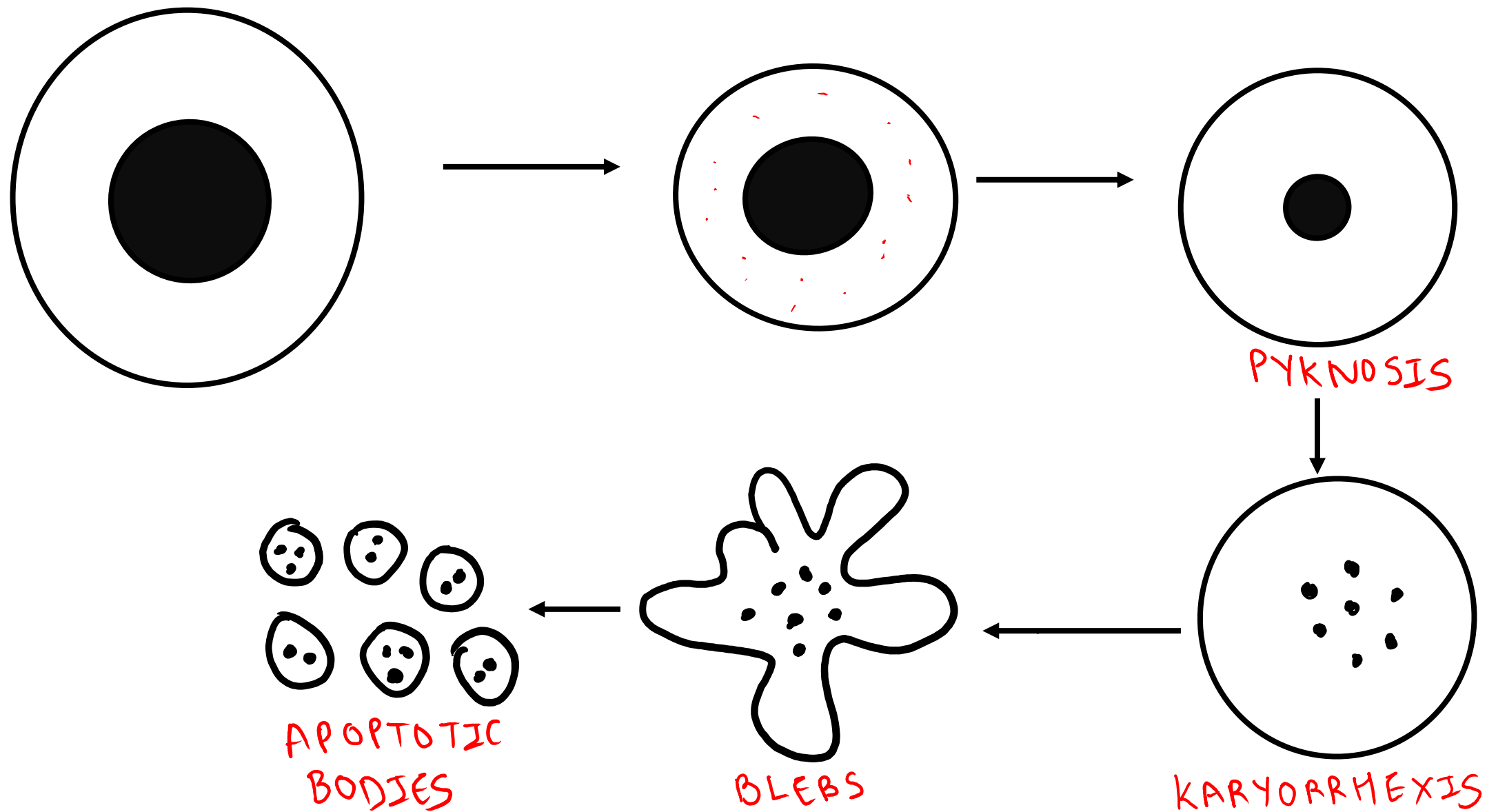


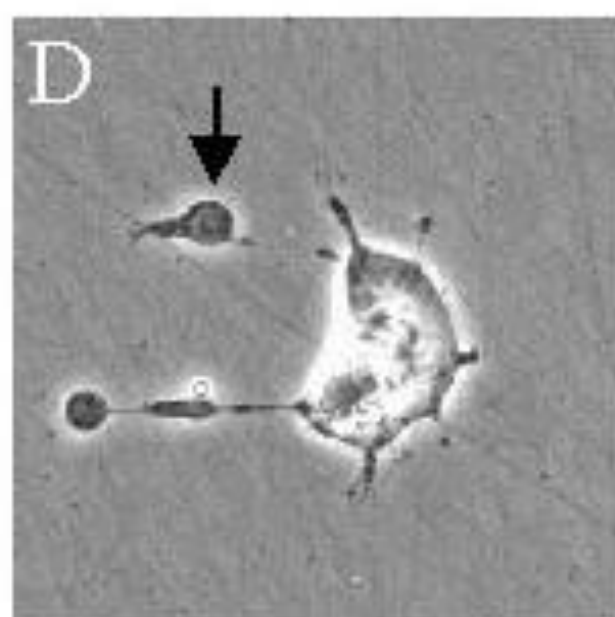
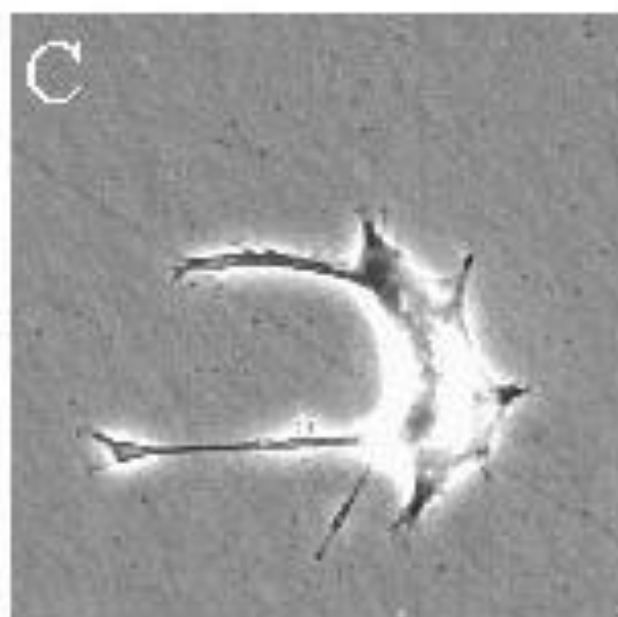
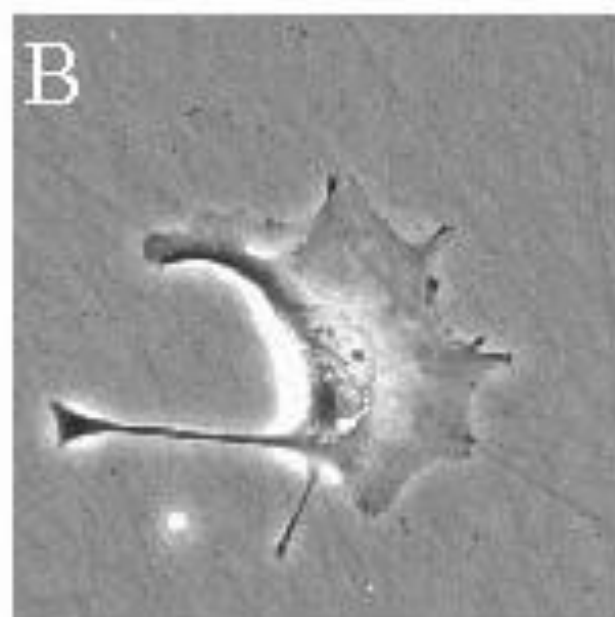
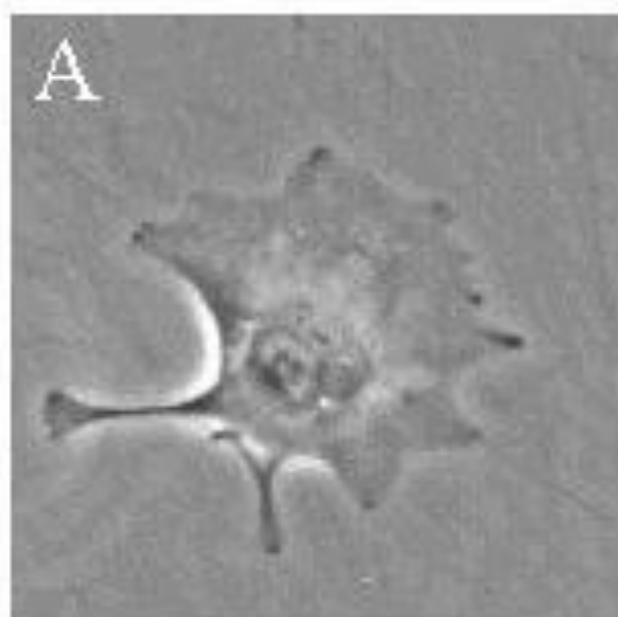
**apoptotic WBC**



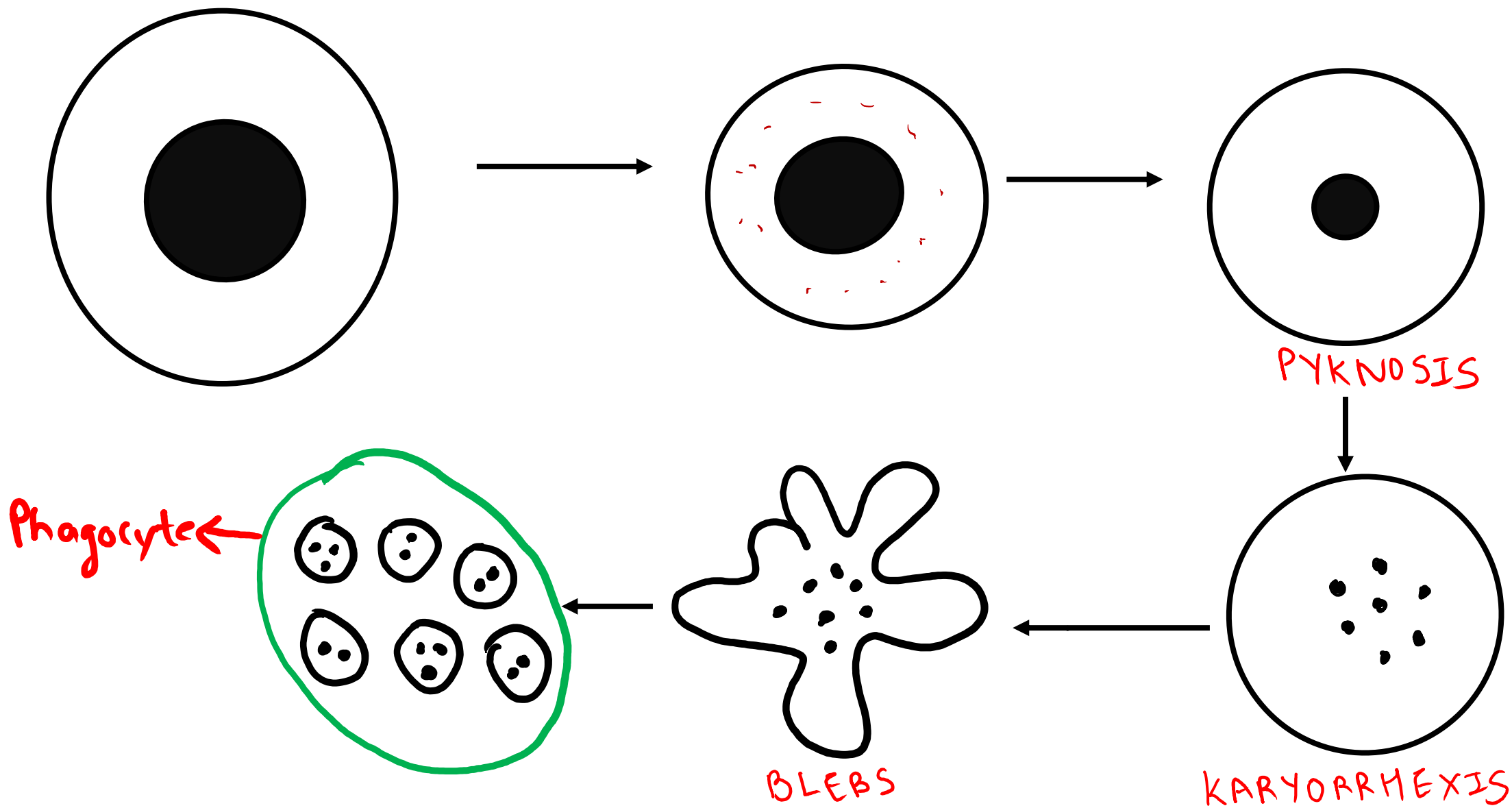
5. Nuclear fragments and cytoplasmic organelles form membrane bound **apoptotic bodies**

- These are membrane bound round masses of eosinophilic cytoplasm with tightly packed organelles which may contain nuclear debris





- These apoptotic bodies are recognised by **phagocytes** and **destroyed**
- Characteristically, unlike necrosis, there is **no acute inflammatory reaction** around apoptosis.



# POLLS

*Scan or Click to watch  
Cell Adaptation & Injury*



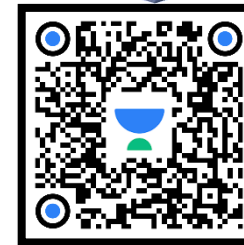
*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*





# **The earliest change seen in apoptosis is**

- **a) Cell shrinkage**
- **b) Pyknosis**
- **c) Formation of apoptotic bodies**
- **d) Fragmentation of cells**

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# **Characteristic feature of apoptosis**

- **a) Cell membrane intact**
- **b) Cytoplasmic Basophilia**
- **c) Nuclear moulding**
- **d) Cell swelling**

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# **All of the following are features of apoptosis EXCEPT**

- a) Cellular swelling
- b) Nuclear compaction
- c) Intact cell membrane
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# **Apoptotic bodies are**

- **a) Clumped chromatin bodies**
- **b) Pyknotic nucleus without organelles**
- **c) Cell membrane bound with organelles**
- **d) No nucleus with organelles**

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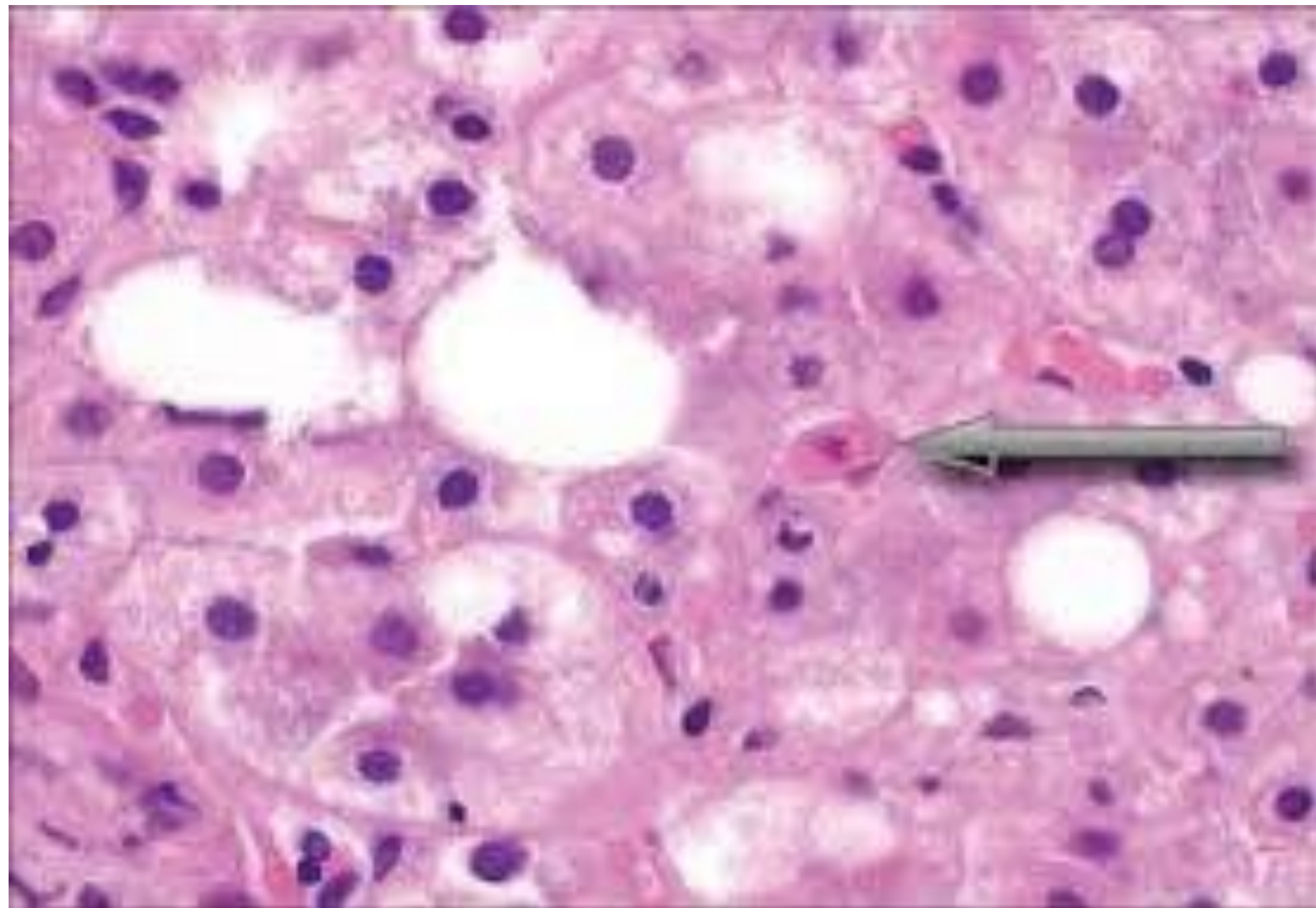
# **OVERVIEW**

- **Definition**
- **Types**
- **Mechanisms**
- **Morphological changes in apoptosis**
- **Diagnosis of Apoptosis**
- **Differences from necrosis**

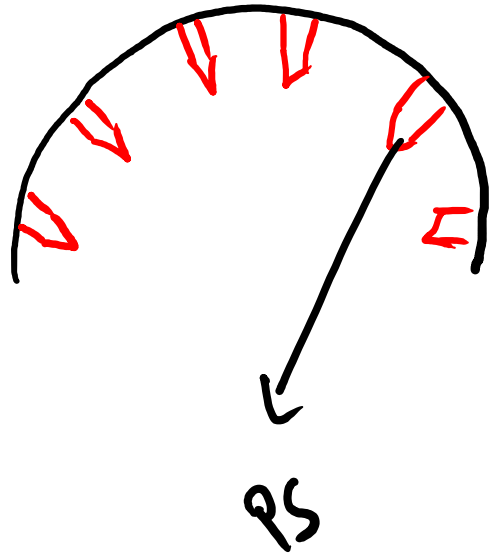
# **DIAGNOSIS OF APOPTOSIS**

# 1. Apoptosis markers

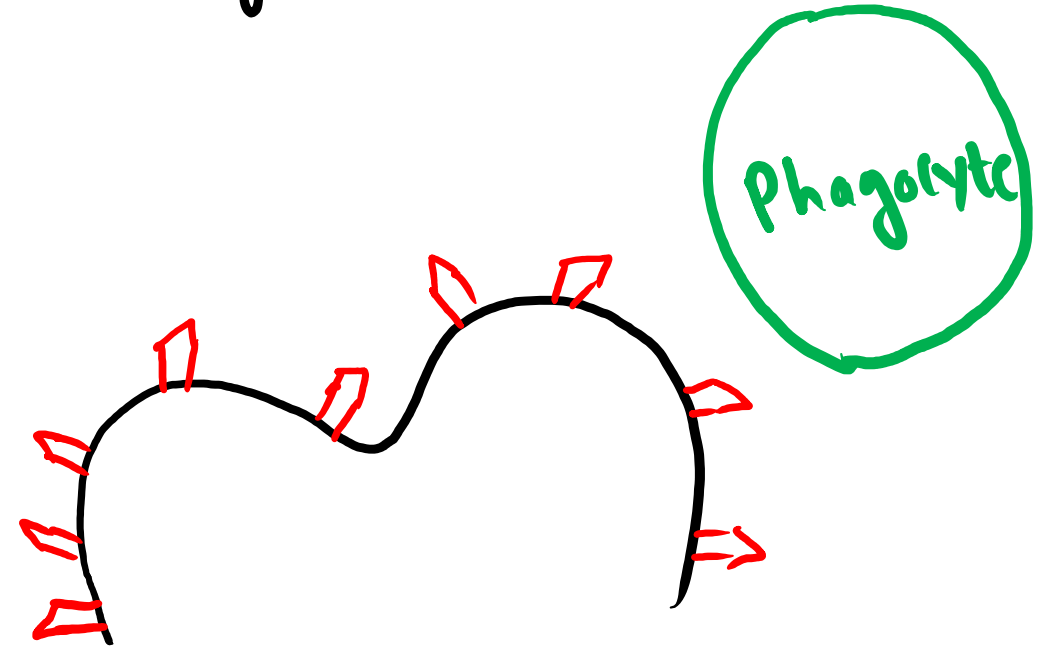
- **Annexin-V** is a recombinant protein with high affinity for phospholipid like phosphatidylserine.
- Phosphatidylserine is a phospholipid present on inner surface membrane normally but it is flipped to outer surface during apoptosis thus become a marker of apoptosis.



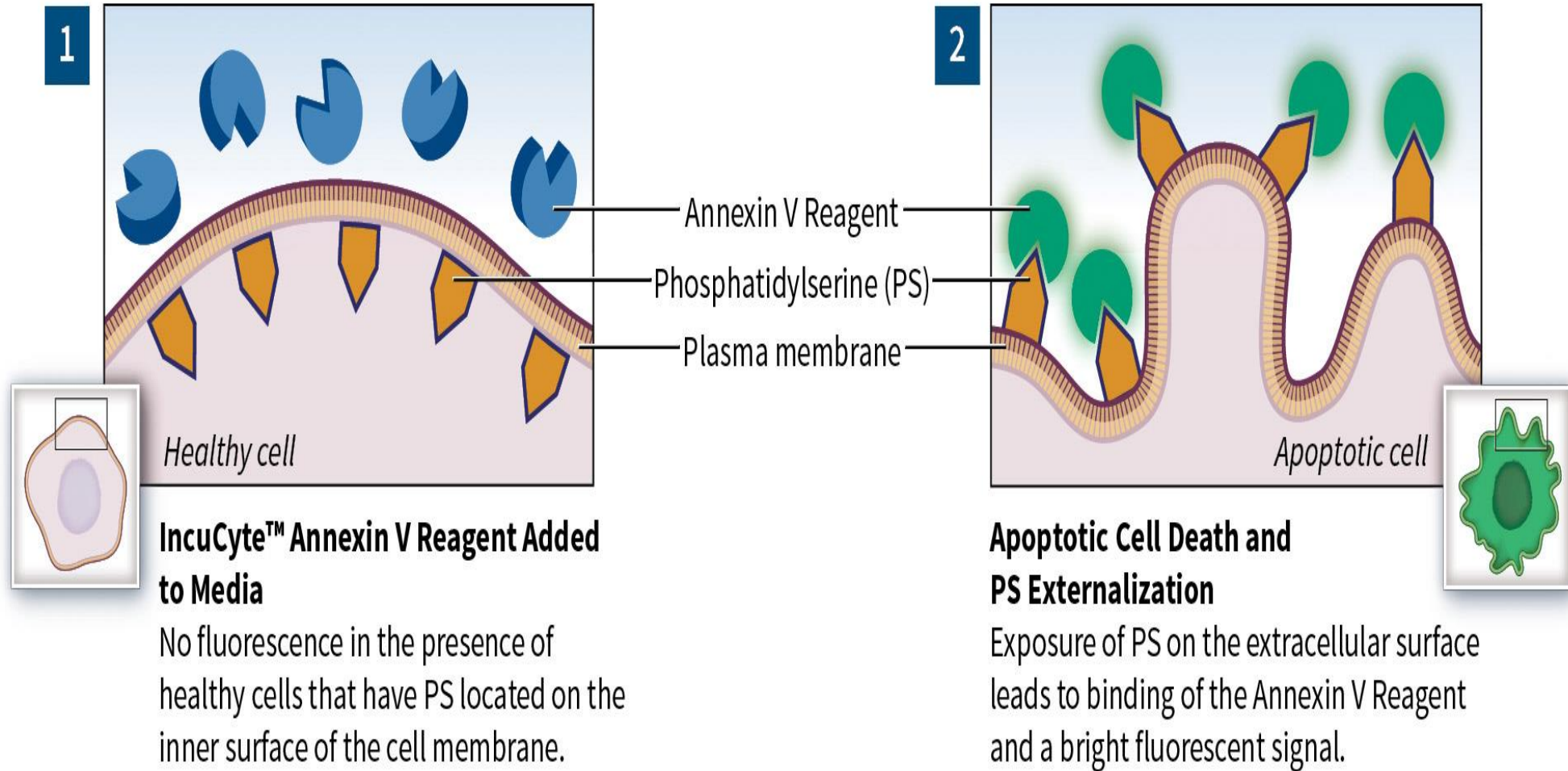
Normally



During apoptosis



## Annexin V overview schematic



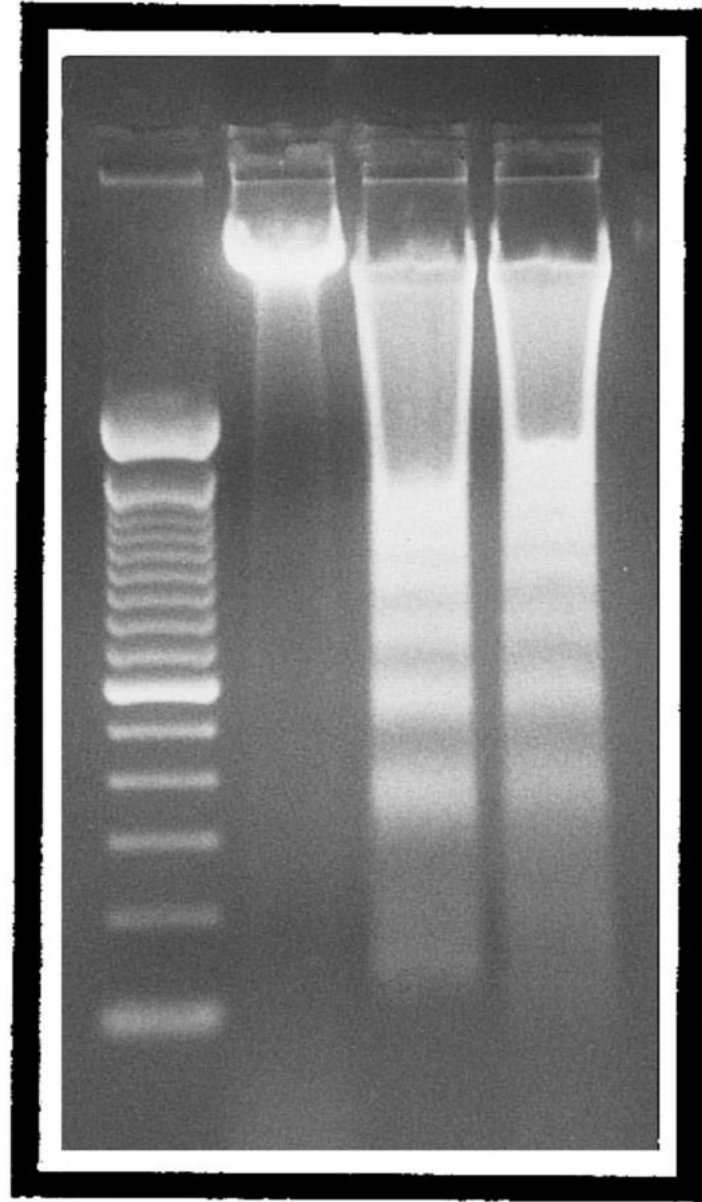
## 2. Agarose gel electrophoresis:

- Fragmented DNA shows **Step Ladder Pattern**, which is due to internucleosomal cleavage of DNA by endonuclease
- During karyorrhexis **endonuclease** activation leaves short DNA fragments regularly spaced in size.
- This ladder pattern is **characteristic but not specific** for apoptosis.

M 1 2 3

1.5 kb →

0.6 kb →





# POLLS

*Scan or Click to watch  
Cell Adaptation & Injury*



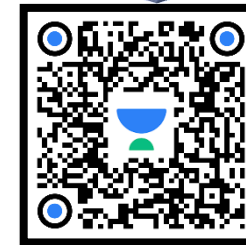
*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*



# **Ladder pattern of DNA electrophoresis in apoptosis is caused by the action of the following enzyme**

- a) Endonuclease
- b) Transglutaminase
- c) DNase
- d) Caspase

# **Ladder pattern of DNA electrophoresis in apoptosis is caused by the action of the following enzyme**

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# **Annexin V is a marker of-**

- **a) Apoptosis**
- **b) Necrosis**
- **c) Artherosclerosis**
- **d) Inflammation**

# **Annexin V is a marker of-**

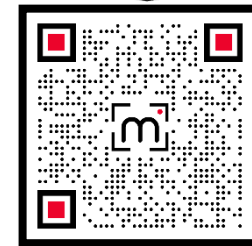
- **a) Apoptosis**
- **b) Necrosis**
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- **d) Inflammation**

# **OVERVIEW**

- **Definition**
- **Types**
- **Mechanisms**
- **Morphological changes in apoptosis**
- **Diagnosis of Apoptosis**
- **Differences from necrosis**

# Differences from necrosis

*Click or Scan QR code to join  
Telegram group discussion*



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## Apoptosis

---

Single cells or small clusters of cells  
Cell shrinkage and convolution  
Pyknosis and karyorrhexis  
Intact cell membrane  
Cytoplasm retained in apoptotic bodies  
No inflammation

---

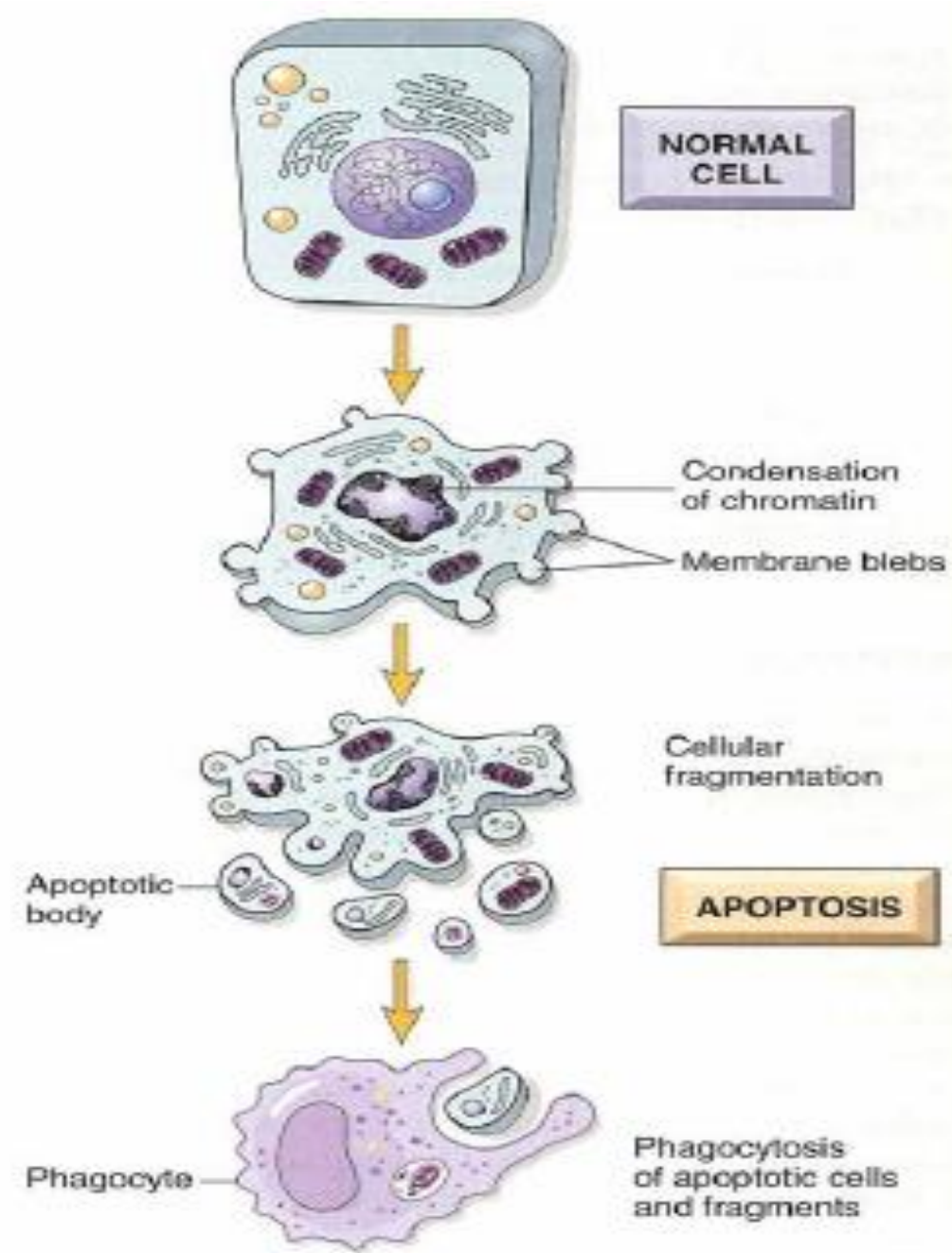
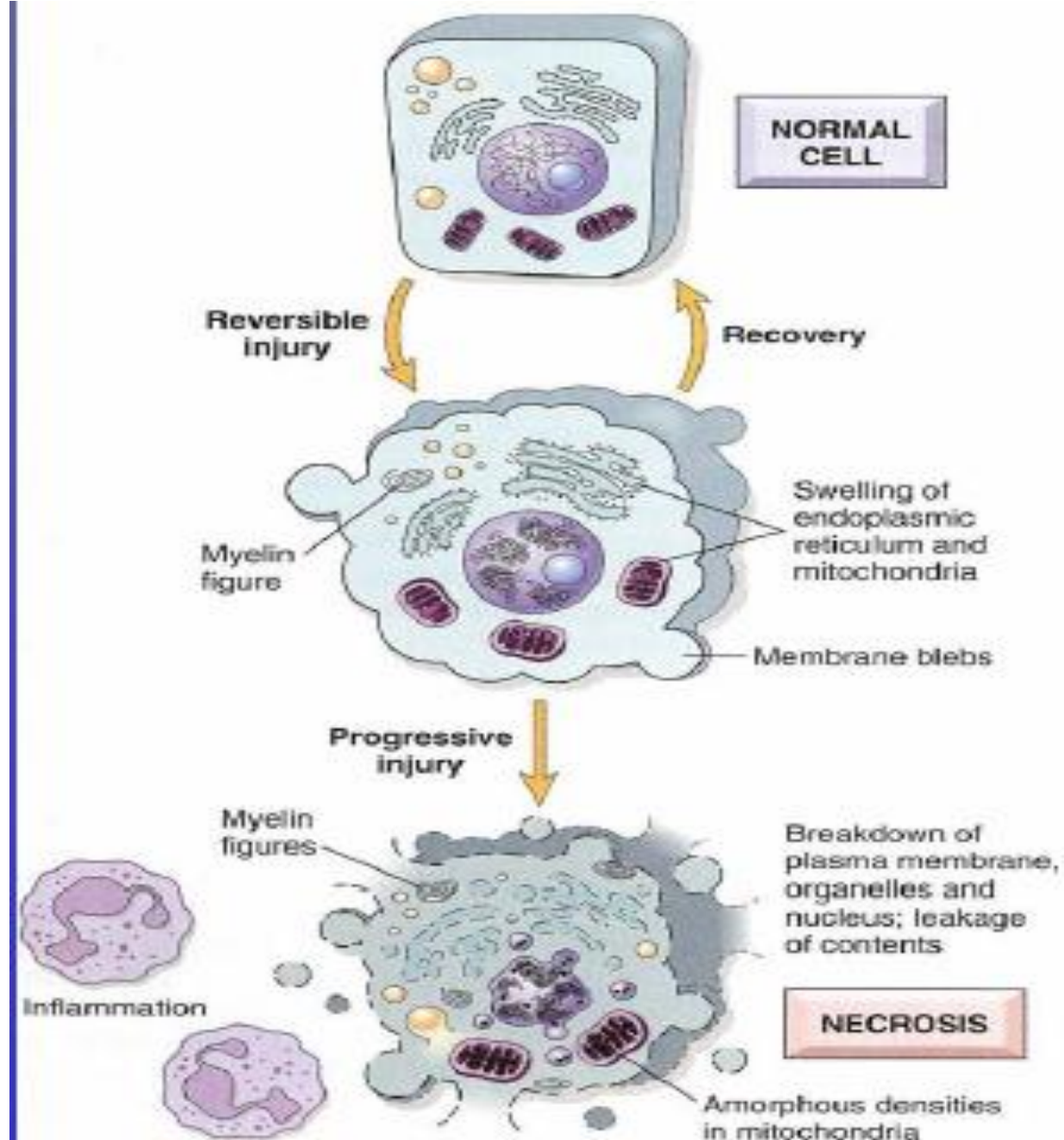
## Necrosis

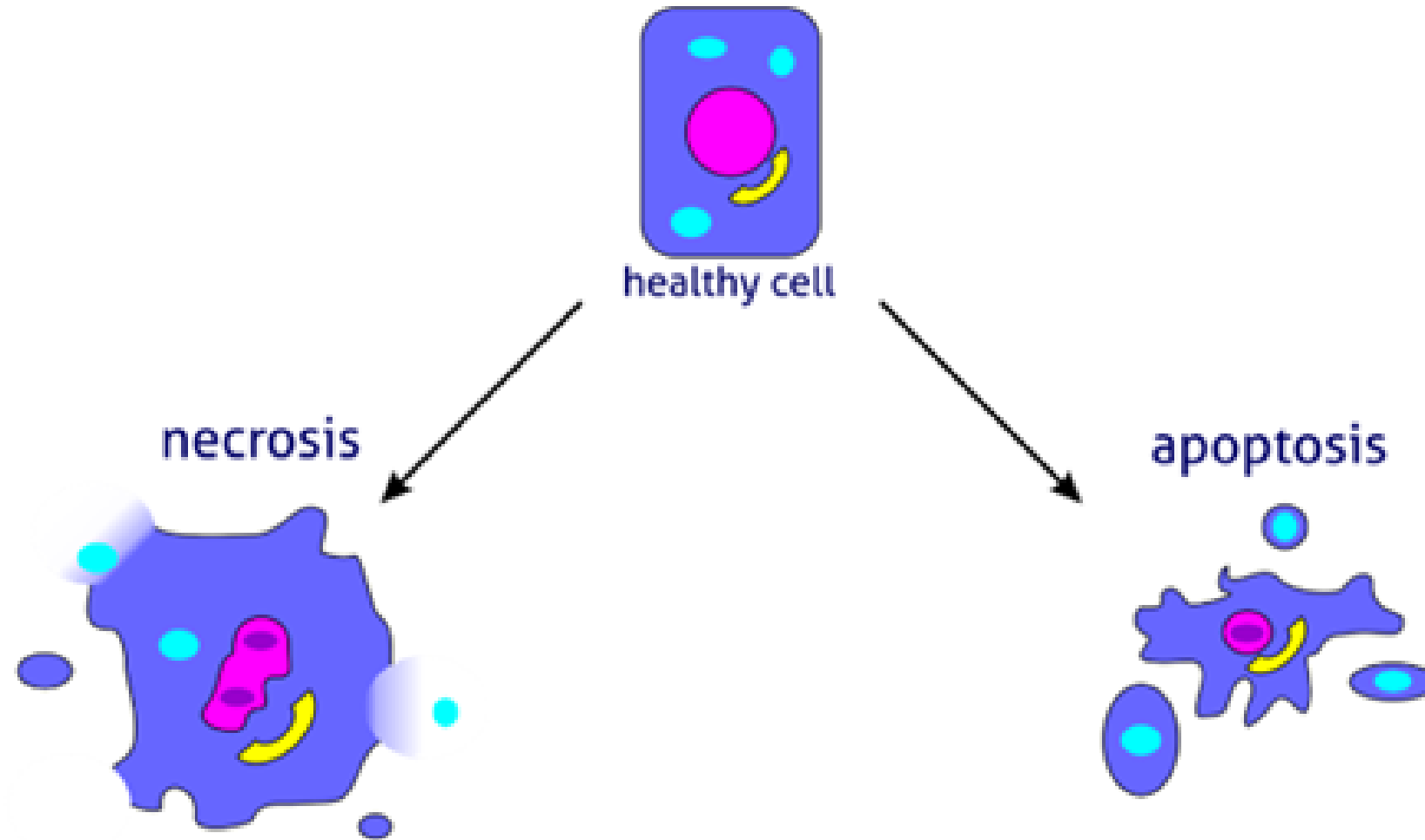
---

Often contiguous cells  
Cell swelling  
Karyolysis, pyknosis, and karyorrhexis  
Disrupted cell membrane  
Cytoplasm released  
Inflammation usually present

---







healthy cell

necrosis

apoptosis

- increase in cell volume
- loss of plasma membrane integrity
- leakage of cellular contents

- cell shrinkage
- plasma membrane blebbing
- formation of apoptotic bodies

# POLLS

*Scan or Click to watch  
Cell Adaptation & Injury*



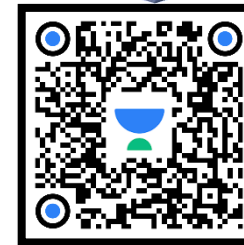
*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*



# **What is the common change in cell death associated with both apoptosis and necrosis?**

- a) Cell shrinkage
- b) Bleb formation
- c) Chromatin condensation
- d) Presence of inflammation

# **What is the common change in cell death associated with both apoptosis and necrosis?**

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# **Apoptosis is differentiated from necrosis by presence of following feature**

- a) Absence of inflammation
- b) Cell swelling
- c) Disruption of plasma membrane
- d) Passive process

# **Apoptosis is differentiated from necrosis by presence of following feature**

- **a) Absence of inflammation**
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- **c) Disruption of plasma membrane**
- **d) Passive process**

# CELL DEATH

- Apoptosis
- Necrosis



# **NECROSIS**

**Normally cells in homeostasis**



**Physiological and pathological stress**



**Cellular adaptation** (reversible on withdrawal of stimulus)



**If the irritant stimulus persists for long time**



**Cell injury**



**Reversible cell injury**



**Irreversible cell injury** (Cell death)

**-Apoptosis**

**-Necrosis**

# DEFINITION

- Necrosis is **death of cells and tissues in the living animal**
- Necrosis is defined as a **localised area of death of tissue followed later by degradation of tissue by hydrolytic enzymes liberated from dead cells**
- It is invariably accompanied by **inflammatory reaction**

# REMEMBER

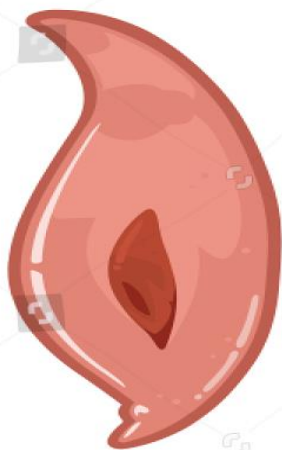
- Necrosis usually affects **a group of contiguous cells** (in contrast to apoptosis which involves a single cell).
- There are **inflammatory changes** in the surrounding tissue (in contrast to apoptosis where there is no inflammatory changes).

# **Types of Necrosis (CCCCFF)**

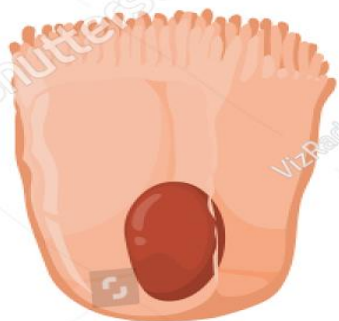
- 5 types→
- Coagulative necrosis (most common)
- Colliquative / Liquefactive necrosis
- Caseous
- Fat necrosis
- Fibrinoid necrosis

- **Introduction**
- **Causes**
- **Gross**
- **Microscopy**





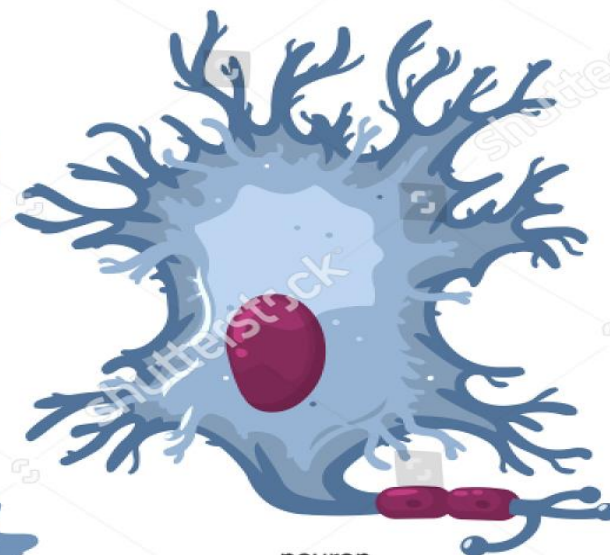
muscle cell



intestinal cell



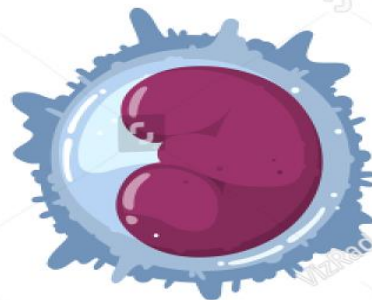
fat cell



neuron



red blood cell



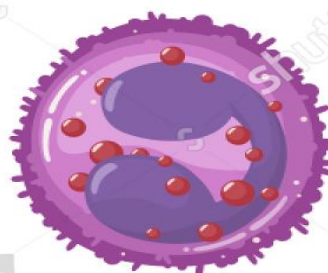
monocyte



basophil



limphocyte



eosinophil



neutrophil



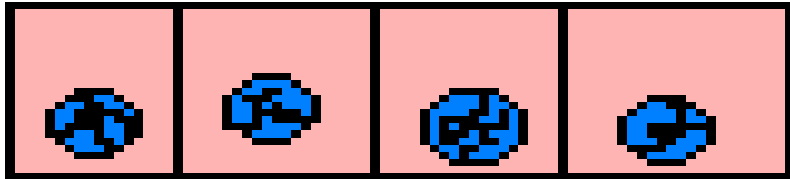
# **Coagulative necrosis**

- **Introduction**
- **Causes**
- **Gross**
- **Microscopy**

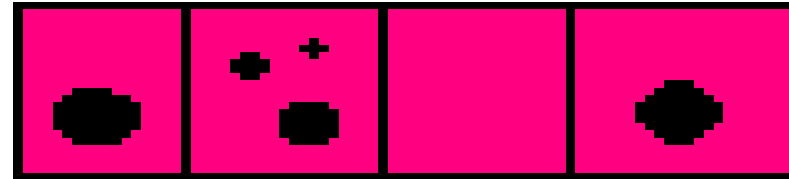
# INTRODUCTION

- **Most common** type of necrosis
- **Architectural outlines persist but cellular and nuclear details are lost (Ghost cells)**
- Type of tissue can be **recognized**
- Denaturation (coagulation) of structural and enzymic proteins blocks proteolysis.

**Alive**



**Coagulation  
Necrosis**



# **Causes:**

- 1. Ischemia** due to thrombosis/ embolism **in all organs except brain** (Amongst solid organs brain is the only exception, i.e., it is the only solid organ in which ischemia leads to liquefactive necrosis and not coagulative necrosis)
2. Mild burns (thermal injury)
3. Zenker's degeneration necrosis

# Grossly

- Focus in the early stage is **pale, firm, and slightly swollen**
- With progression, the affected area becomes **more yellowish, softer, and shrunken.**

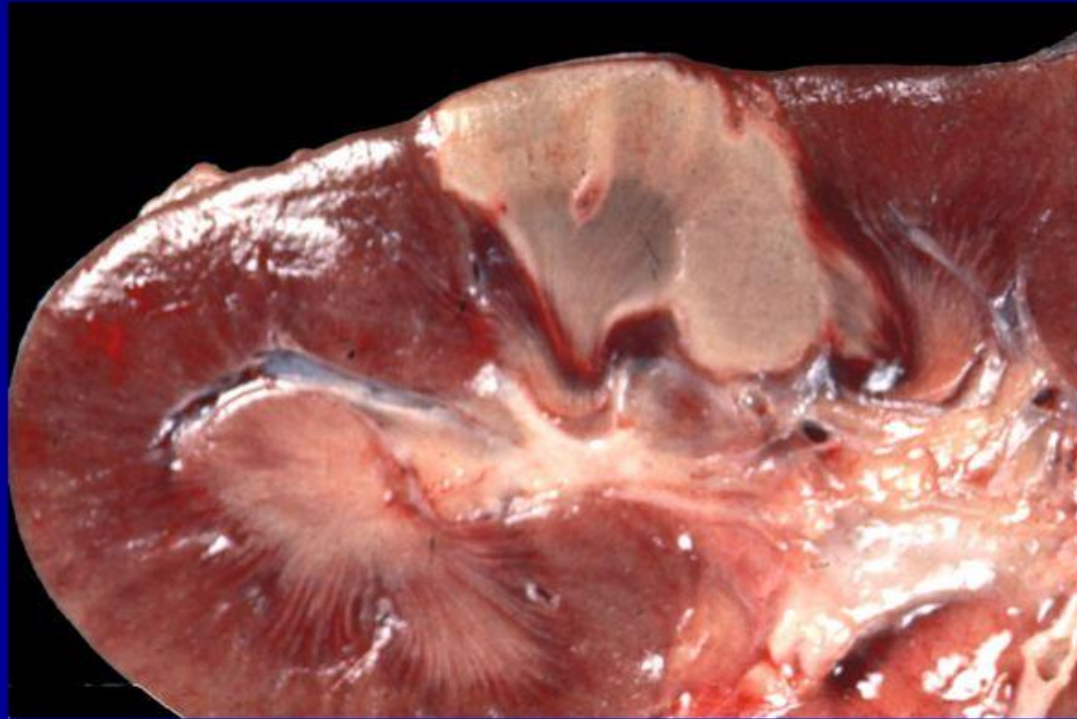






# Coagulative Necrosis

## Kidney - Gross



# Microscopically

- The hallmark of coagulative necrosis is the conversion of normal cells into their '**tomb stones**' i.e. **outlines of the cells are retained and the cell type can still be recognised but their cytoplasmic and nuclear details are lost**

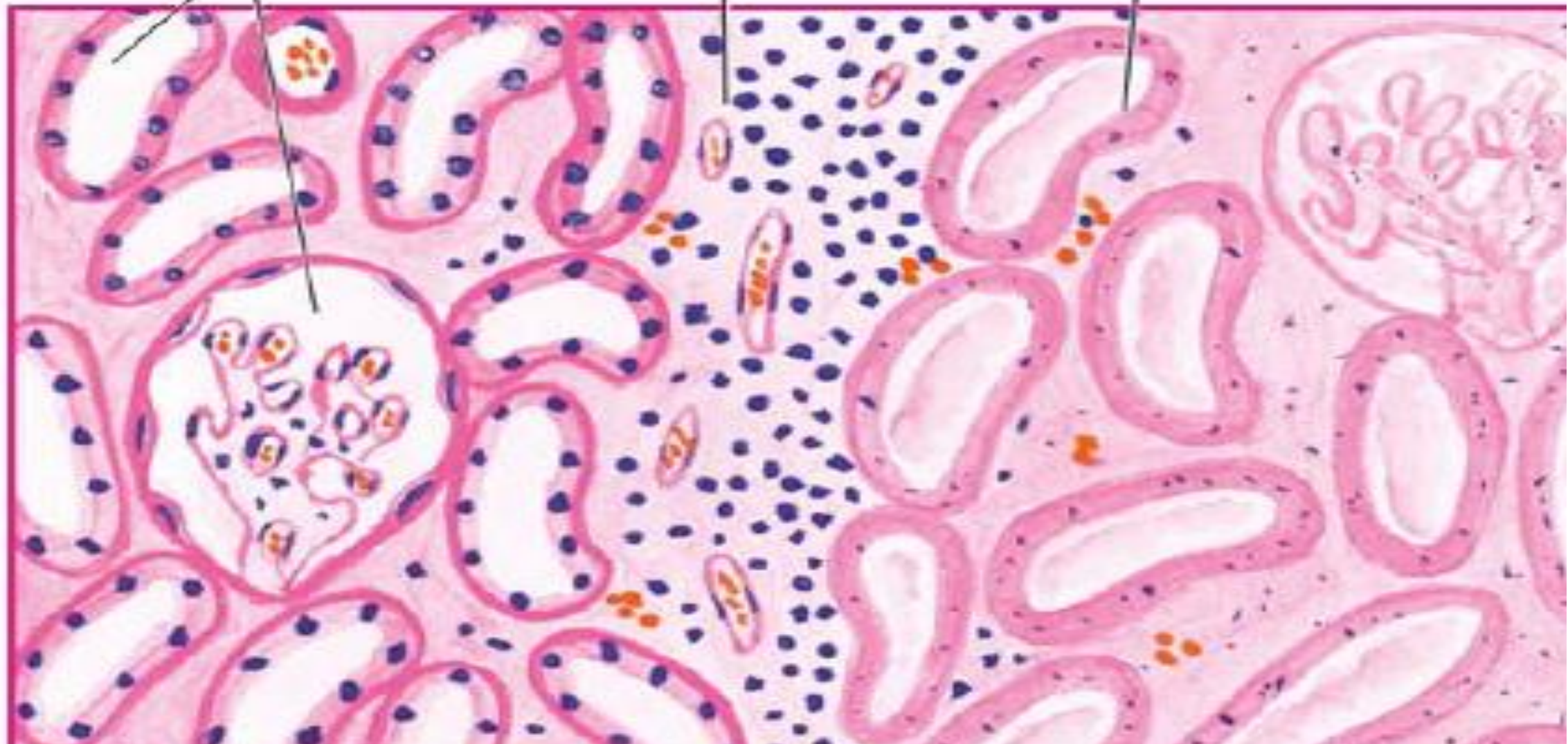




Viable renal tissue

Inflammatory  
cell infiltrate

Necrotic tissue

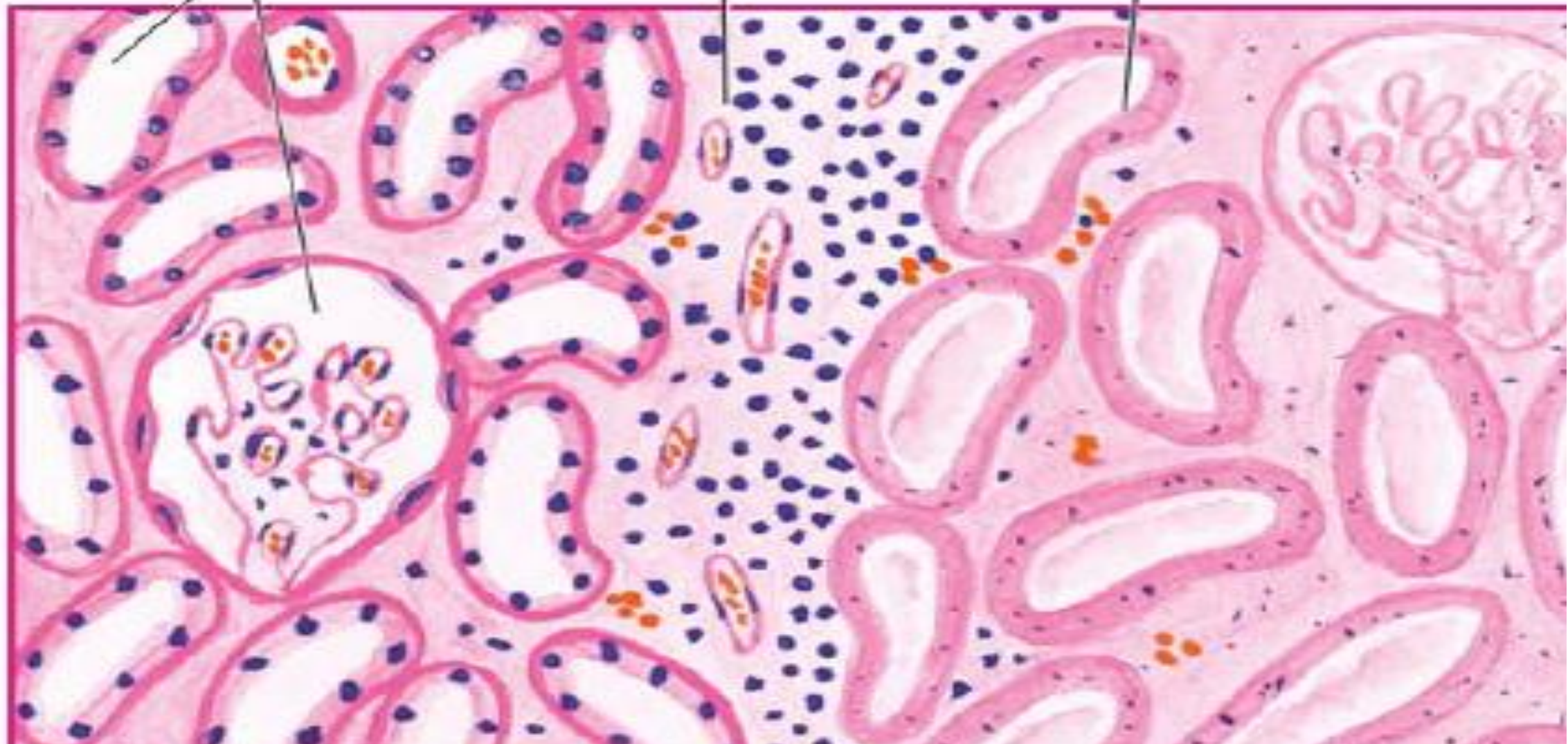




Viable renal tissue

Inflammatory  
cell infiltrate

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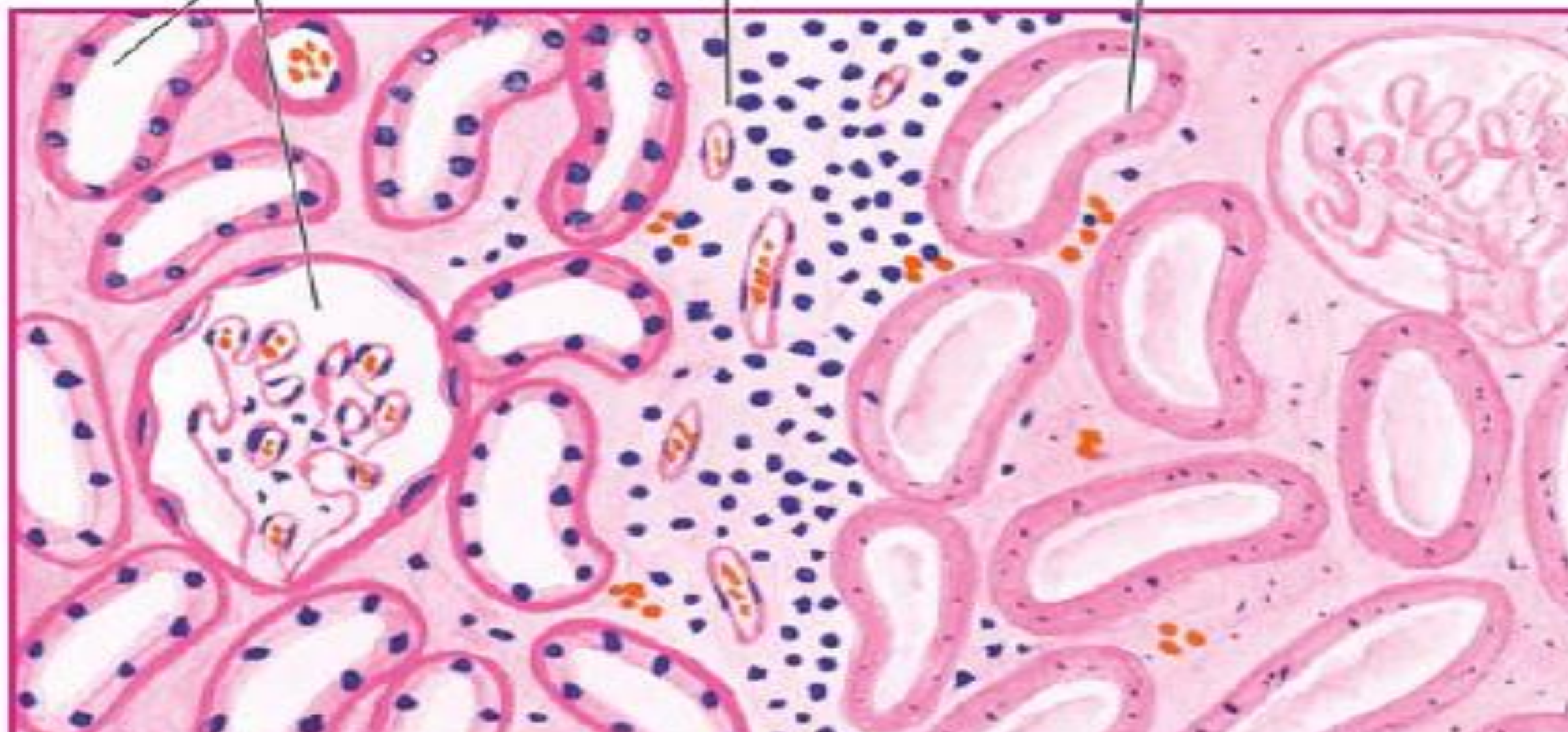
1. **'Tomb stones'** i.e. **outlines of the cells are retained and the cell type can still be recognised but their cytoplasmic and nuclear details are lost**
2. The necrosed cells are **swollen and have more eosinophilic cytoplasm** than the normal.
3. These cells show **nuclear changes of pyknosis, karyorrhexis and karyolysis**
4. Eventually, the necrosed focus is infiltrated by **inflammatory cells**



Viable renal tissue

Inflammatory  
cell infiltrate

Necrotic tissue

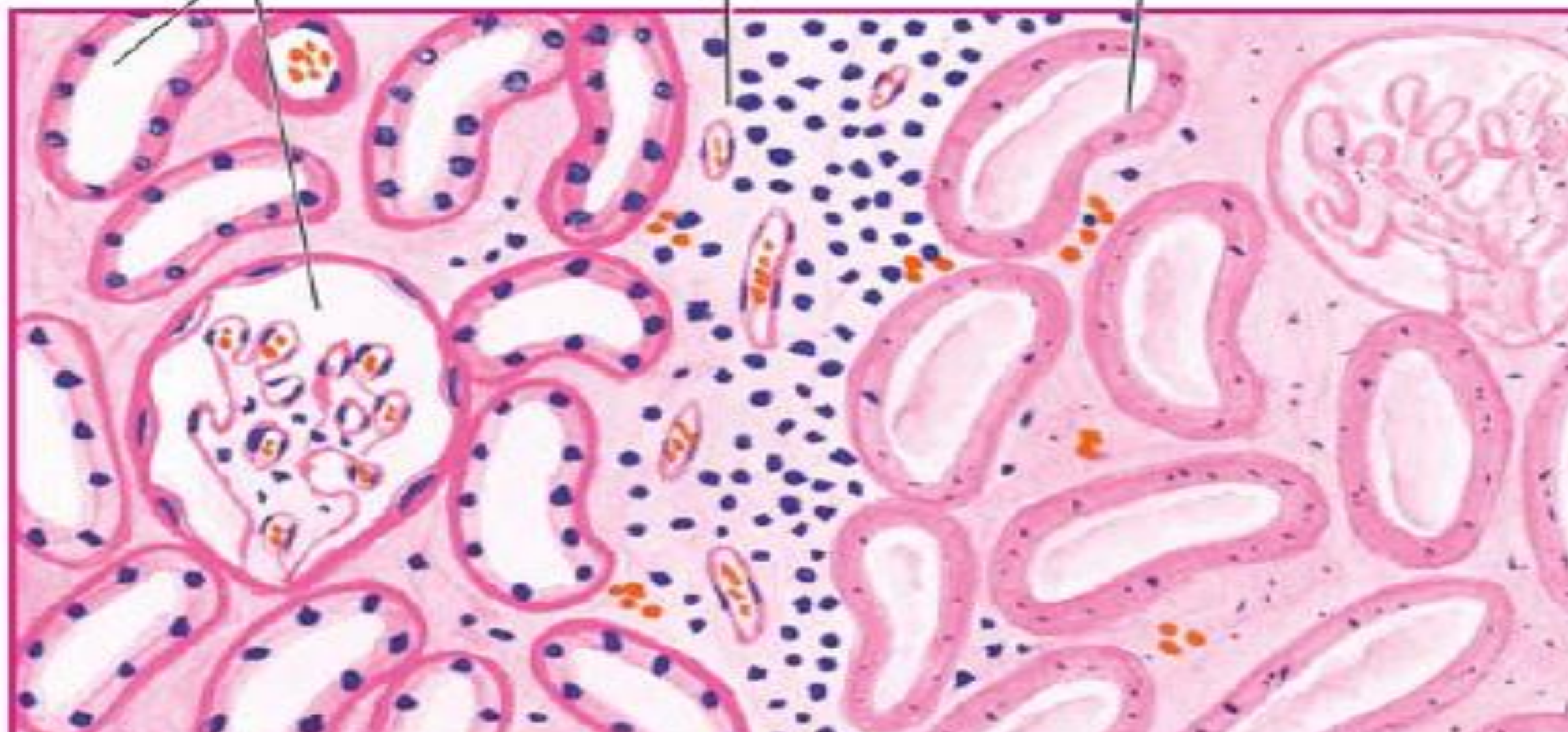




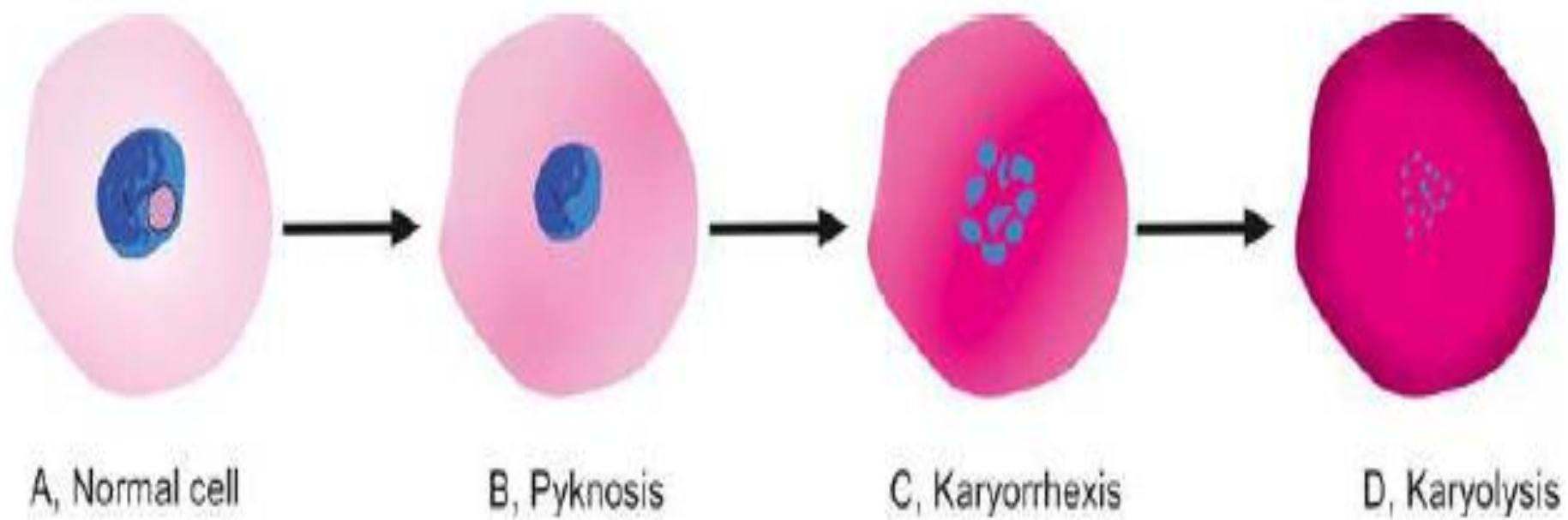
Viable renal tissue

Inflammatory  
cell infiltrate

Necrotic tissue







# **Types of Necrosis (CCCCFF)**

- 5 types→
- Coagulative necrosis (most common)
- Colliquative / Liquefactive necrosis
- Caseous
- Fat necrosis
- Fibrinoid necrosis

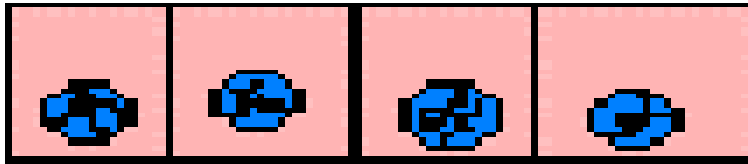
# **Liquefactive (COLLIQUATIVE) necrosis**

- **Introduction**
- **Causes**
- **Gross**
- **Microscopy**

# INTRODUCTION

- Liquefaction or colliquative necrosis → hydrolytic enzymes in tissue degradation have a dominant role in causing **semi-fluid material**
- **Their architectural details as well as cytoplasmic and nuclear details are lost**

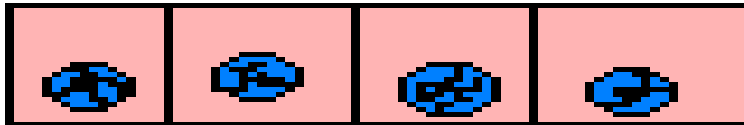
**Alive**



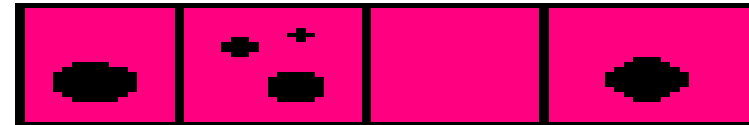
**Liquefaction  
Necrosis**



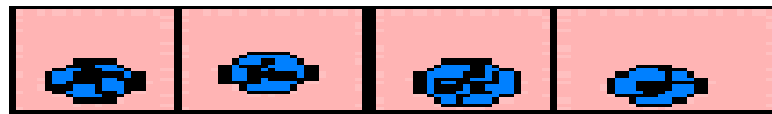
**Alive**



**Coagulation  
Necrosis**



**Alive**



**Liquefaction  
Necrosis**



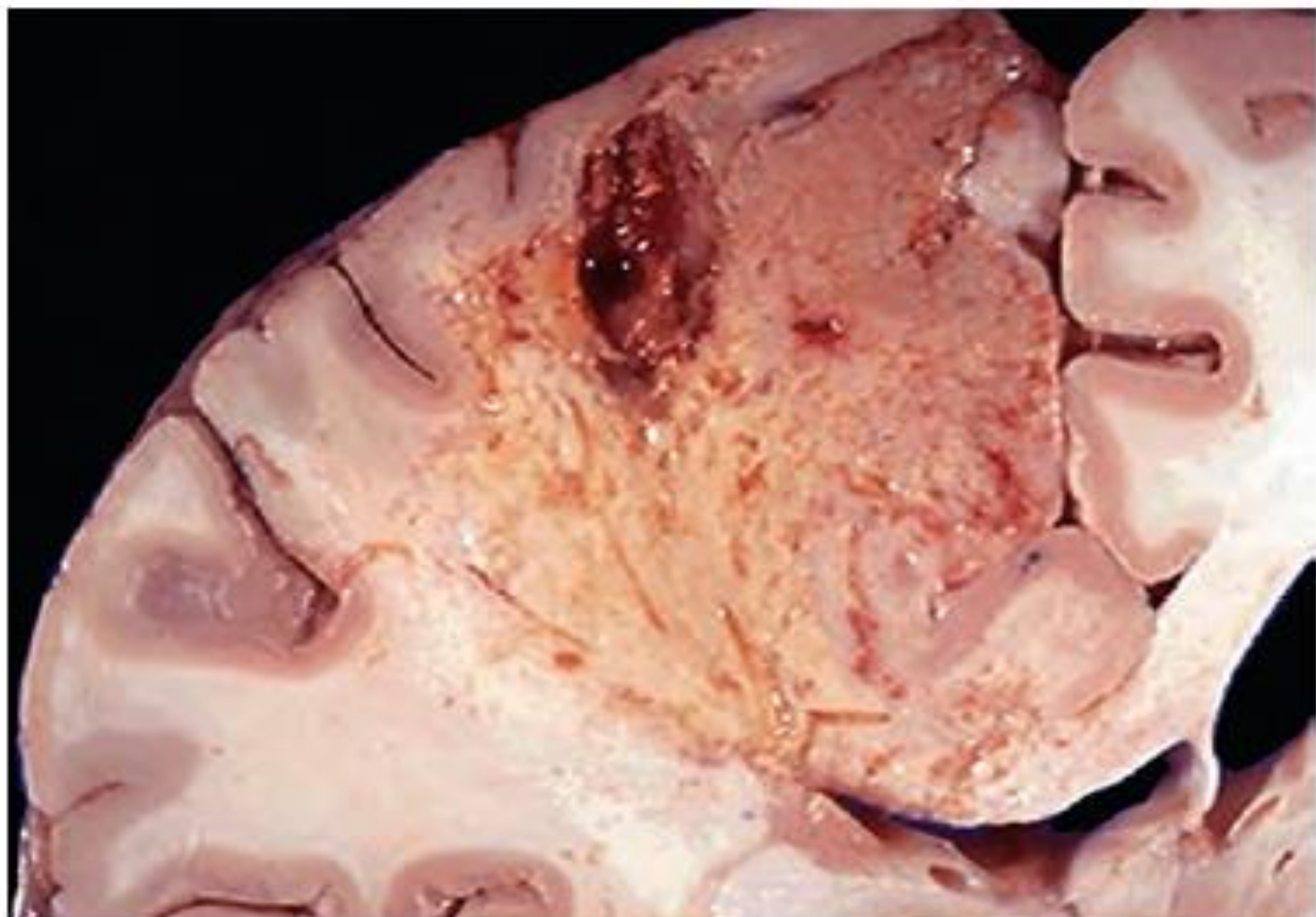
# Causes:

1. **Pyogenic bacterial infections** attract neutrophils.  
Bacterial and leukocytic enzymes liquefy dead cells and tissues.
2. **Ischemic necrosis of brain**



# Gross appearance

- Affected area is **soft with liquefied centre containing necrotic debris**
- Later, a **cyst wall** is formed.



# Microscopic appearance:

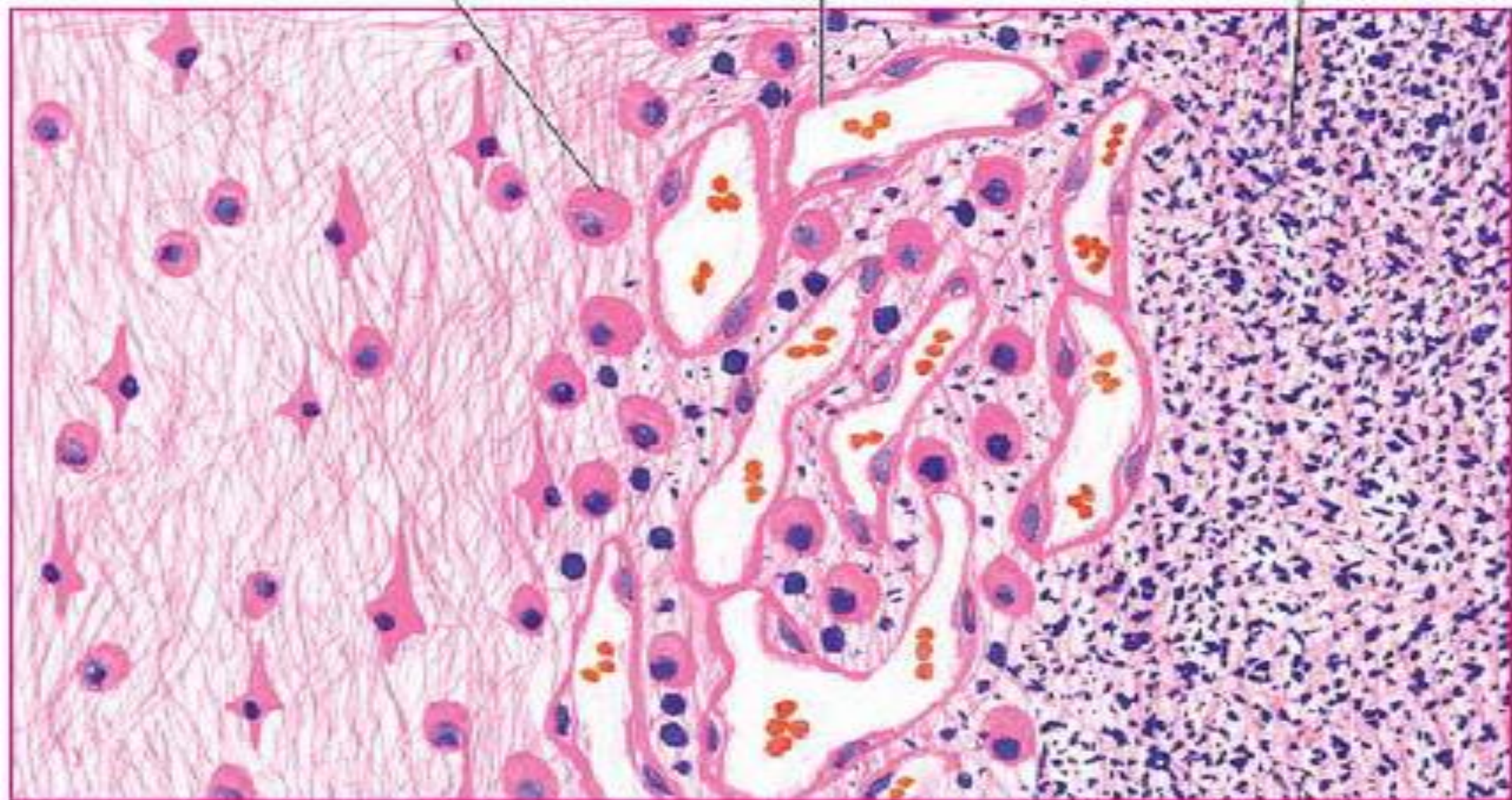
1. No architectural or cellular details are visible in the area of necrosis.
2. The necrotic area usually appears as a cavity containing a mass of necrotic neutrophils, bacteria and tissue debris
3. The entire necrotic mass is surrounded by a fibrous connective tissue capsule/cyst wall
4. The cyst wall is formed by proliferating capillaries, inflammatory cells, and gliosis



Gliosis

Granulation tissue

Liquefactive necrosis



# **Types of Necrosis (CCCCFF)**

- 5 types→
- Coagulative necrosis (most common)
- Colliquative / Liquefactive necrosis
- Caseous
- Fat necrosis
- Fibrinoid necrosis

# **Caseous necrosis (cheese like)**

- **Introduction**
- **Causes**
- **Gross**
- **Microscopy**

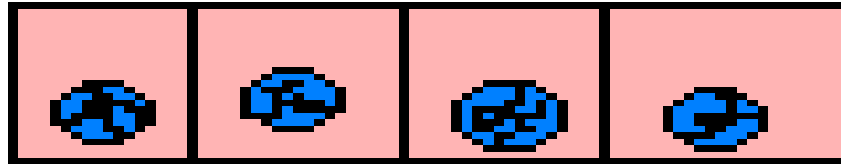
# INTRODUCTION

- Dead tissue is converted into a **homogenous, granular mass resembling cottage cheese.**
- **Their architectural details as well as cytoplasmic and nuclear details are lost**
- **Accumulation of amorphous (no structure) debris within an area of necrosis**

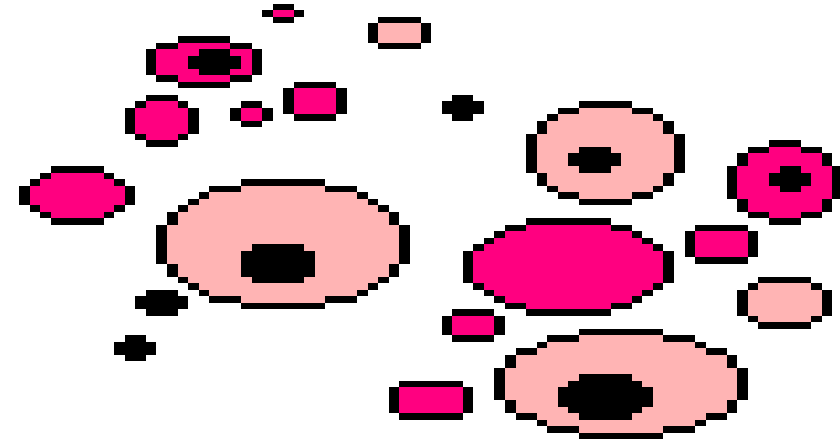




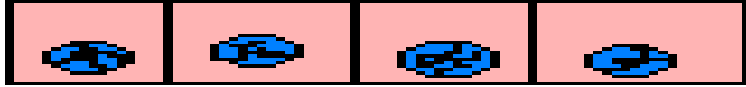
**Alive**



**Caseous  
Necrosis**



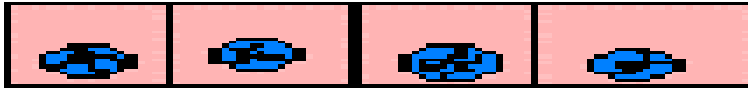
**Alive**



**Coagulation  
Necrosis**



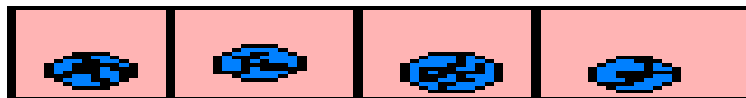
**Alive**



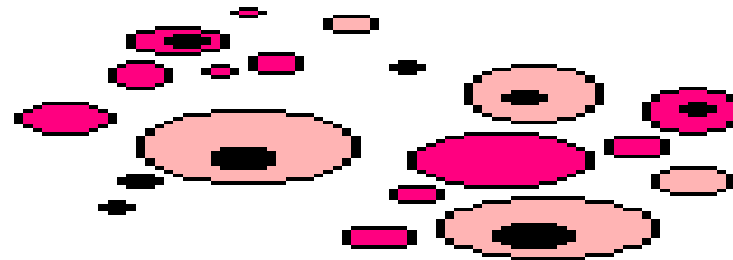
**Liquefaction  
Necrosis**



**Alive**



**Caseous  
Necrosis**



# Cause:

- Associated with lesions of **Mycobacterium tuberculosis, syphilis and fungi (Histoplasma , Coccidioidomycosis)**

# Gross appearance

- Foci of caseous necrosis resemble **dry cheese and are soft, granular and yellowish.**
- This appearance is partly attributed to the histotoxic effects of **lipopolysaccharides present in the capsule of the tubercle bacilli, Mycobacterium tuberculosis**



**Figure 2-13** Caseous necrosis. Tuberculosis of the lung, with a large area of caseous necrosis containing yellow-white and cheesy debris.

# Microscopically

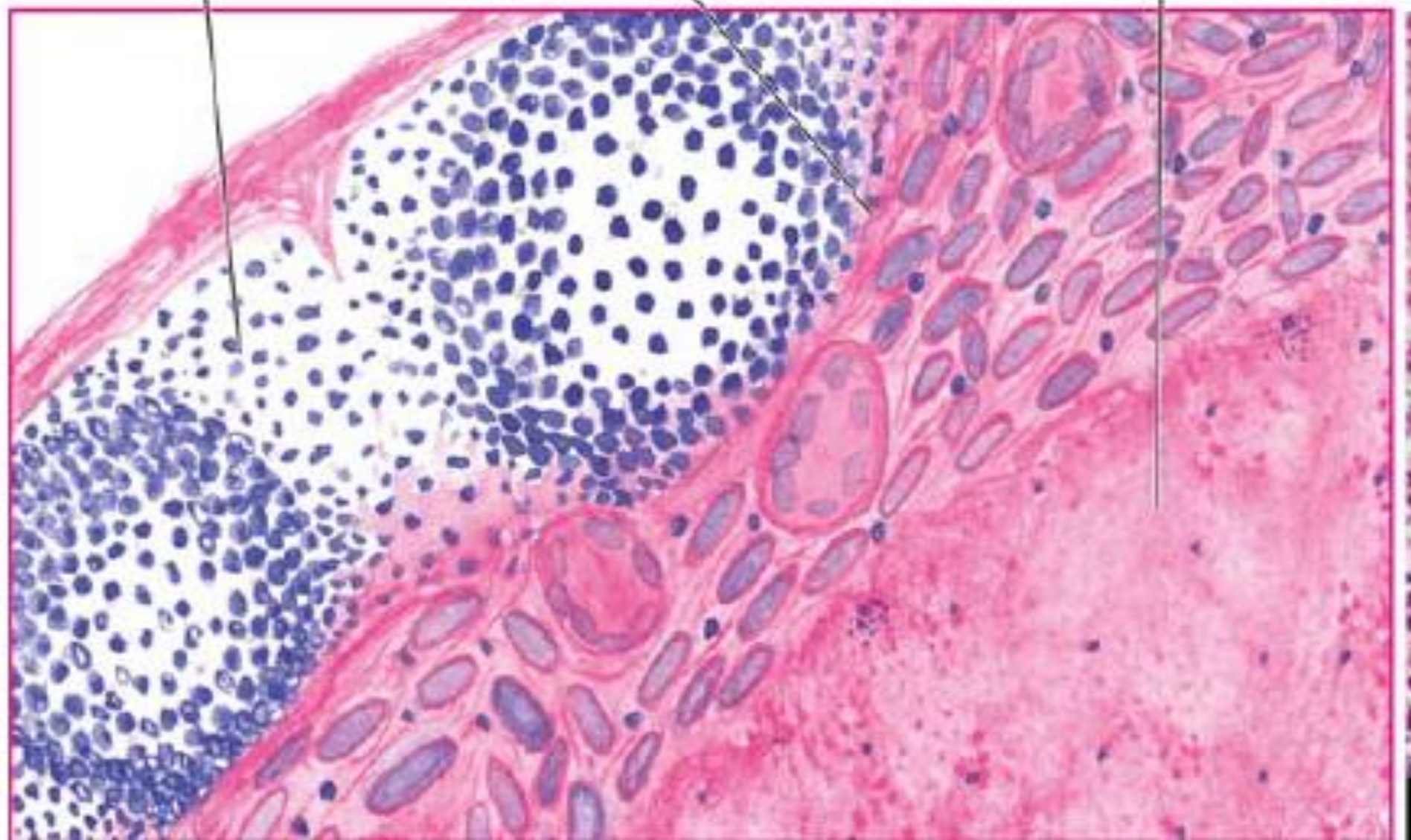
- **Centre** of the necrosed focus contain **structureless, eosinophilic material having scattered granular debris of disintegrated nuclei**
- The **surrounding tissue** shows characteristic **granulomatous inflammatory reaction** consisting of epithelioid cells (modified macrophages having slipper-shaped vesicular nuclei), interspersed giant cells of Langhans' and foreign body type and peripheral mantle of lymphocytes



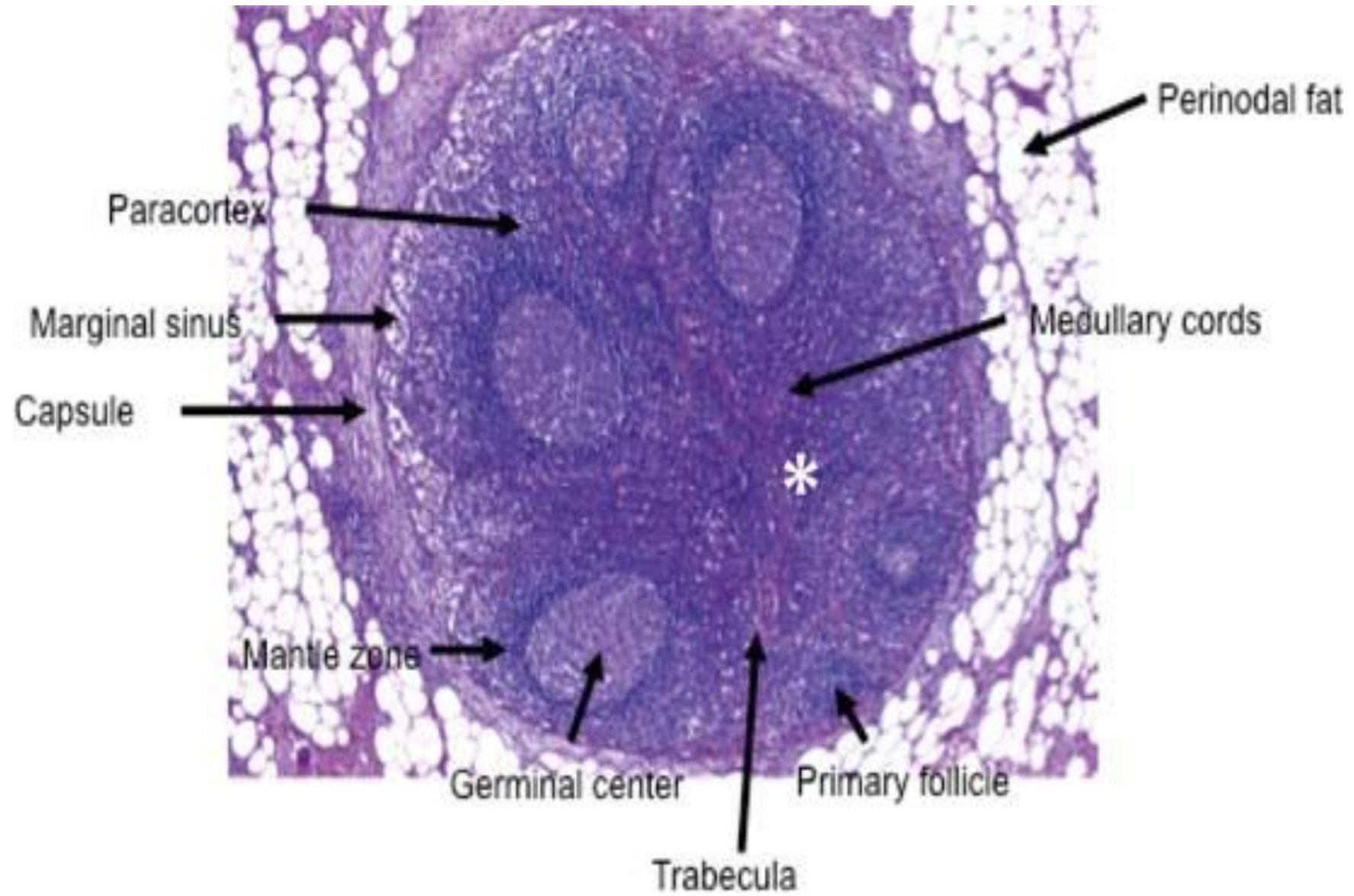
Viable lymphoid tissue

Granulomatous inflammation

Caseous necrosis







# **Types of Necrosis (CCCCFF)**

- 5 types→
- Coagulative necrosis (most common)
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- Caseous
- Fat necrosis
- Fibrinoid necrosis

# **Fat necrosis**

- **Introduction**
- **Causes**
- **Gross**
- **Microscopy**

# INTRODUCTION

- Fat necrosis is a special form of cell death occurring at mainly **fat-rich anatomic locations** in the body.
- **Death of adipose tissue in a living animal**

# **Causes**

- Pancreatic (acute pancreatitis)
- Traumatic (breast)

# Grossly

- Fat necrosis appears as **yellowish-white and firm deposits.**
- Formation of calcium soaps imparts the necrosed foci firmer and **chalky white appearance**

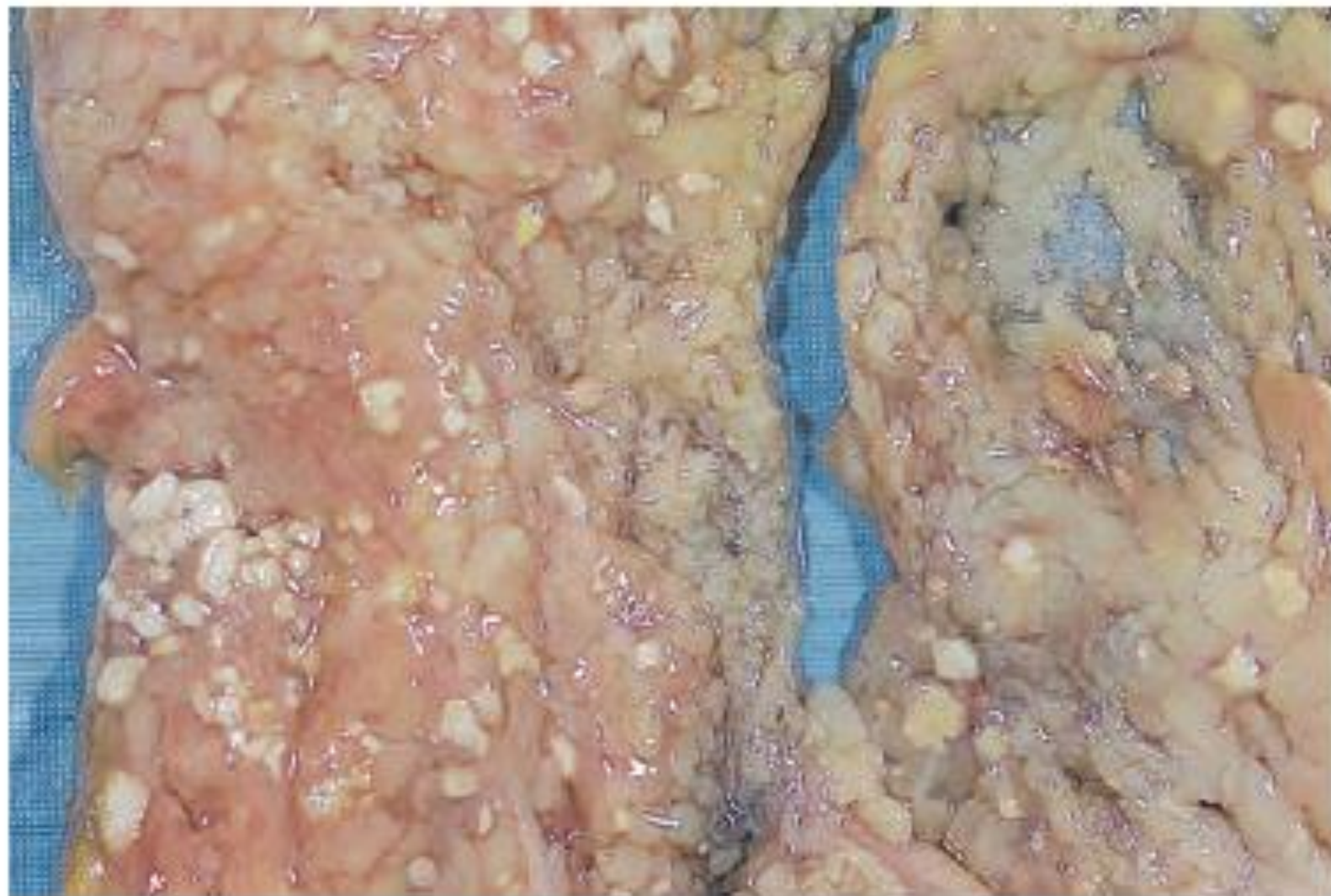


Figure 2-14 Fat necrosis. The areas of white chalky deposits represent foci of fat necrosis with calcium soap formation (saponification) at sites of lipid breakdown in the mesentery.





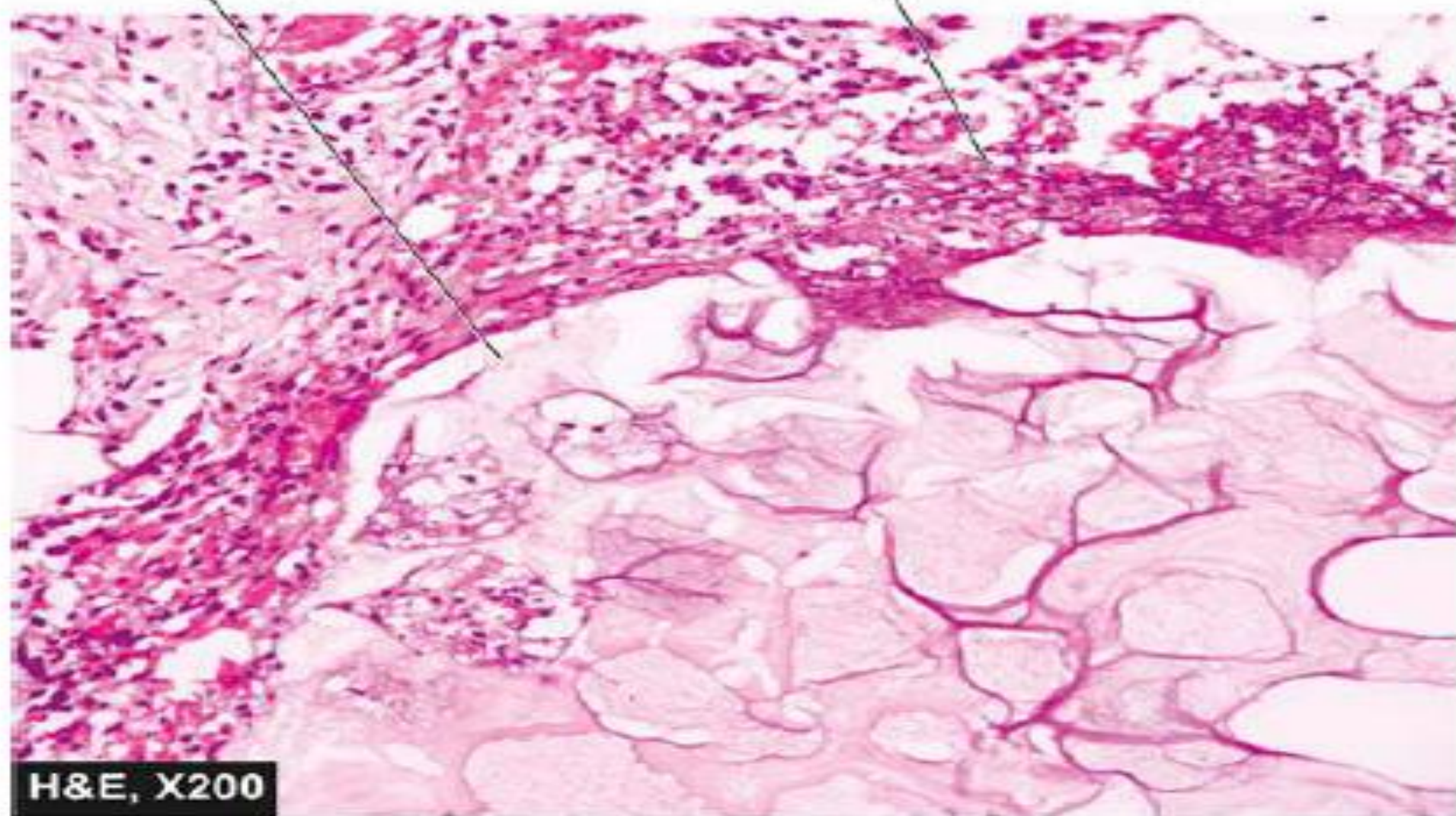
# Microscopically

- The necrosed fat cells have **cloudy appearance**
- They are surrounded by an **inflammatory reaction.**
- Formation of calcium soaps is identified in the tissue sections as **amorphous, granular and basophilic material**



Cloudy appearance

Mixed inflammatory cells



H&E, X200

# **Types of Necrosis (CCCCFF)**

- 5 types→
- Coagulative necrosis (most common)
- Colliquative / Liquefactive necrosis
- Caseous
- Fat necrosis
- Fibrinoid necrosis

# Fibrinoid Necrosis

- Fibrinoid necrosis is characterized by **deposition of fibrin-like material** which has the staining properties of fibrin
- The fibrin like material is deposited in **wall of blood vessels**

# Causes

- **Immunologic injury of vessel wall** (e.g. in immune complex vasculitis, autoimmune diseases, Arthus reaction etc), arterioles in hypertension, peptic ulcer etc.

# Microscopically

- Fibrinoid necrosis is identified by **brightly eosinophilic, hyaline-like deposition in the vessel wall.**
- Necrotic focus is surrounded by **nuclear debris of neutrophils (leucocytoclasia)**
- **Local haemorrhage** may occur due to rupture of the blood vessel.



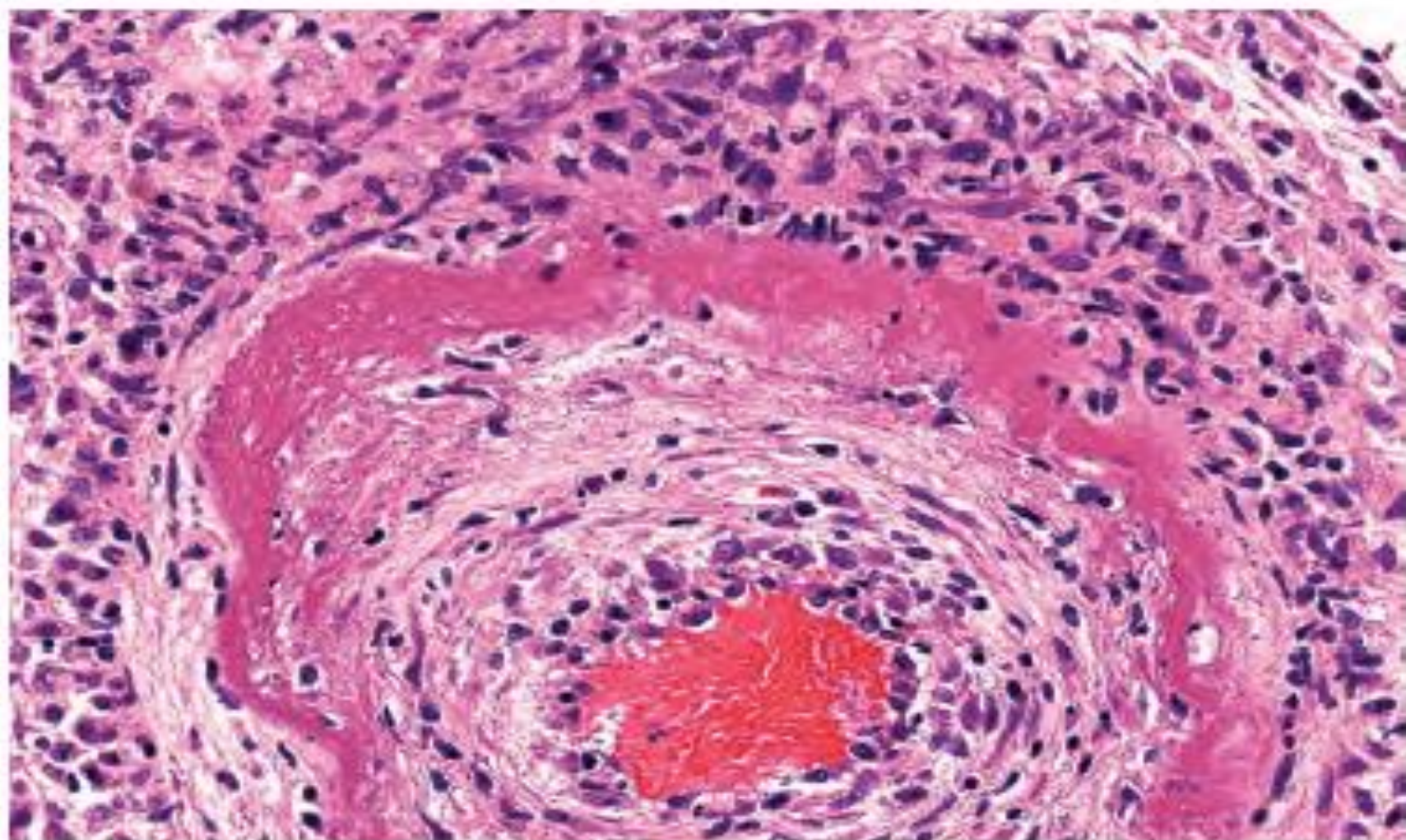


Figure 2-15 Fibrinoid necrosis in an artery. The wall of the artery shows a circumferential bright pink area of necrosis with inflammation (neutrophils with dark nuclei).



# REVISION

# **Types of Necrosis (CCCCFF)**

- 5 types→
- Coagulative necrosis (most common)
- Colliquative / Liquefactive necrosis
- Caseous
- Fat necrosis
- Fibrinoid necrosis

Viable renal tissue

Inflammatory  
cell infiltrate

Necrotic tissue

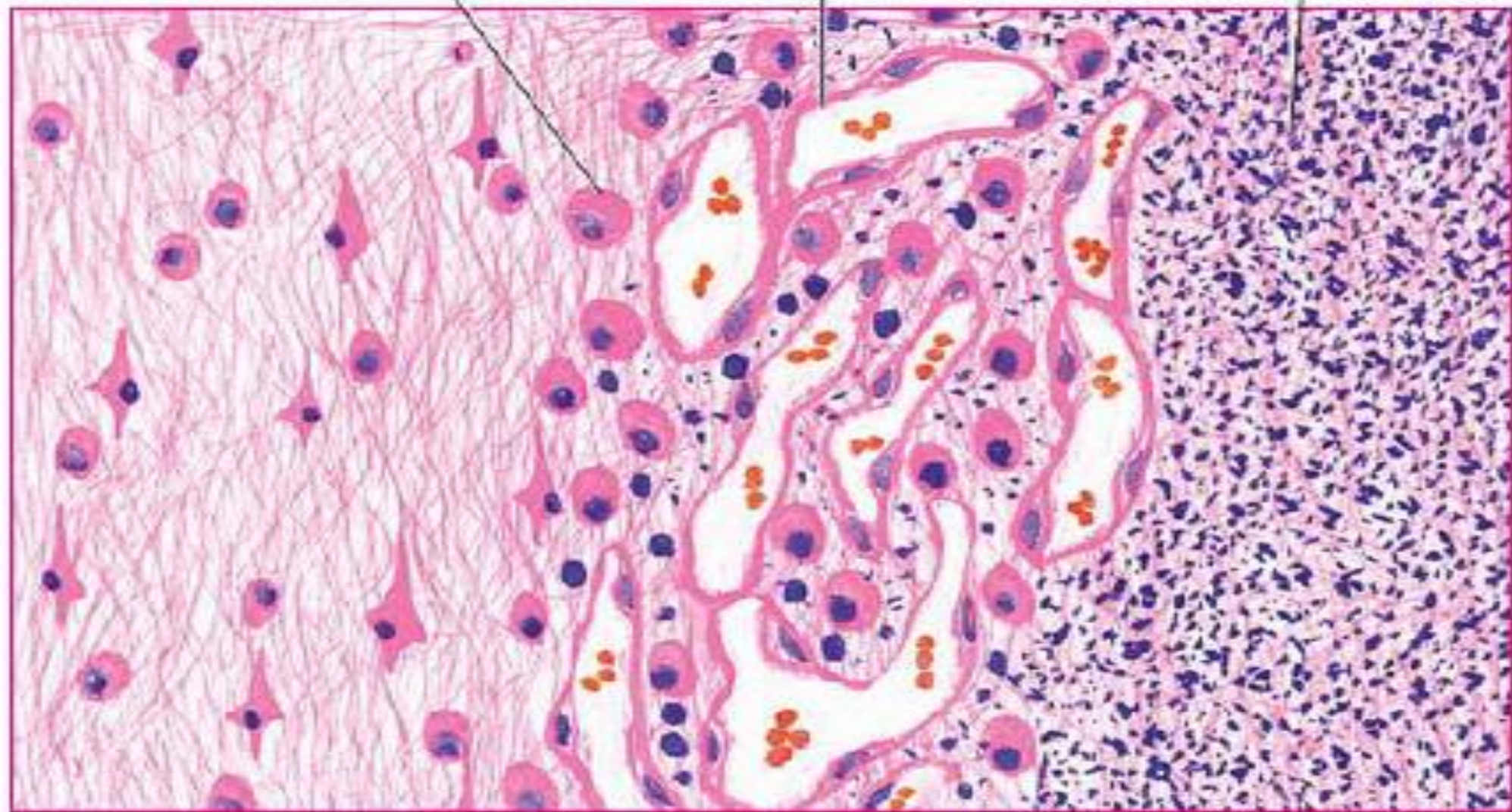




Gliosis

Granulation tissue

Liquefactive necrosis

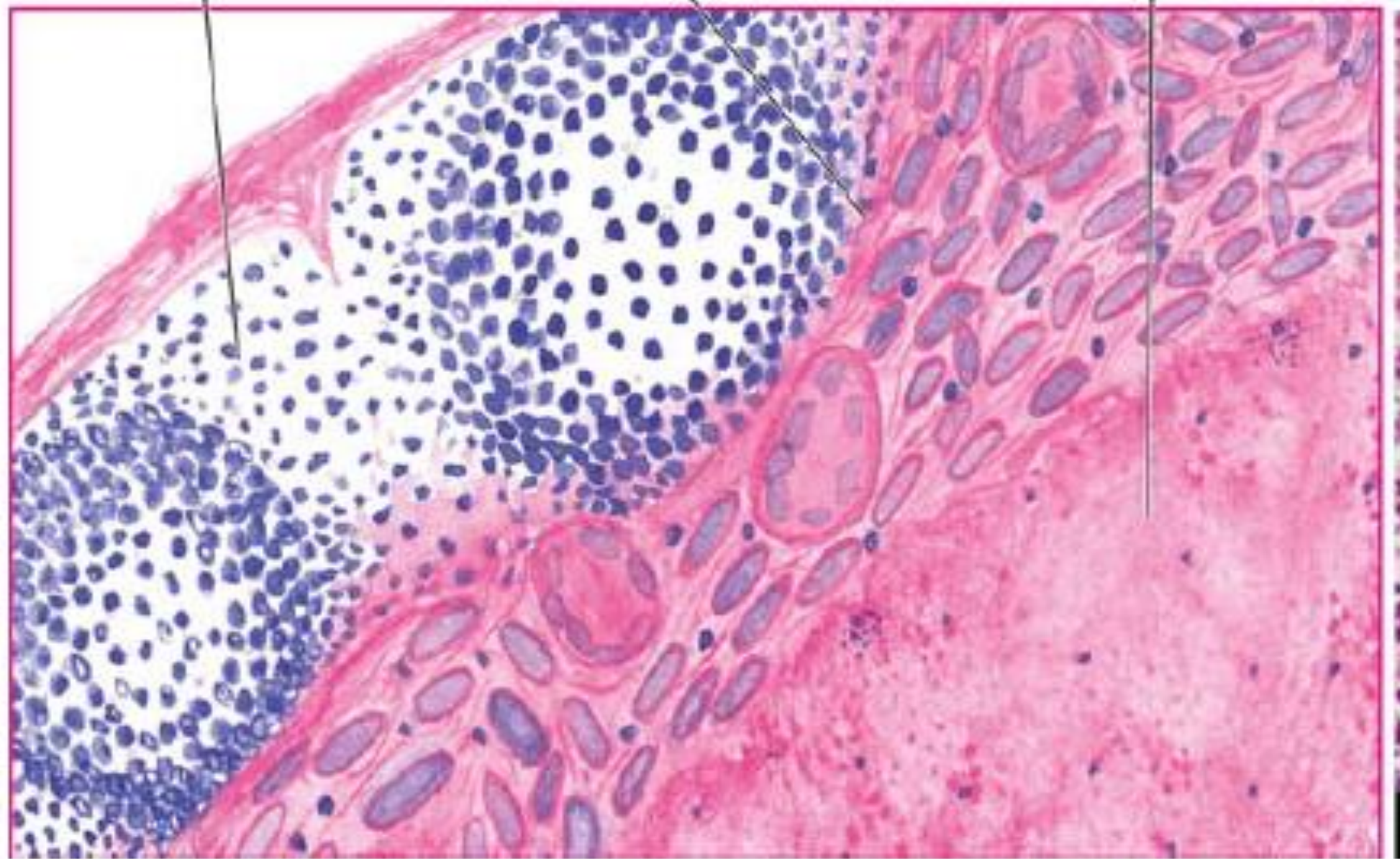




Viable lymphoid tissue

Granulomatous inflammation

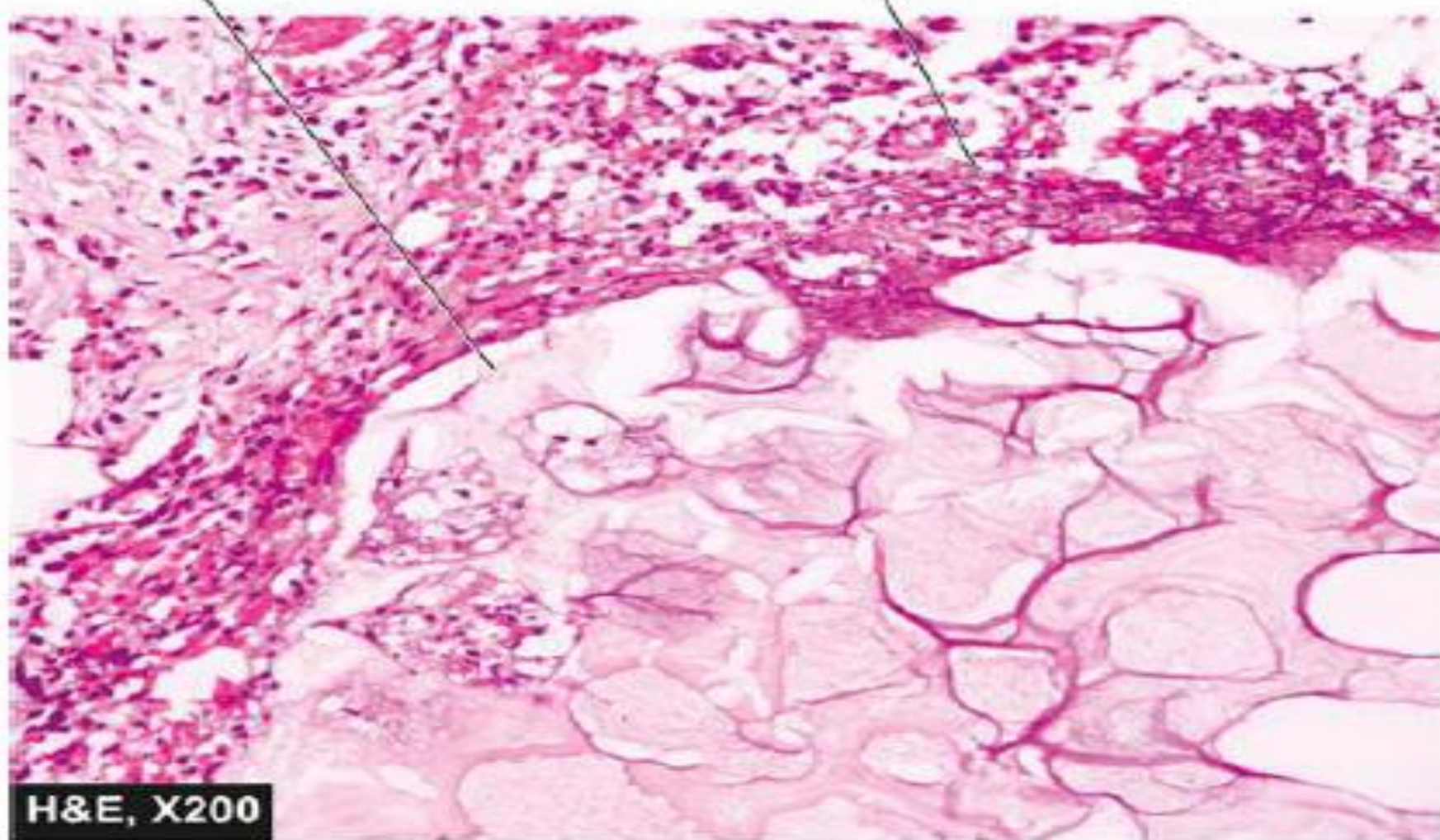
Caseous necrosis





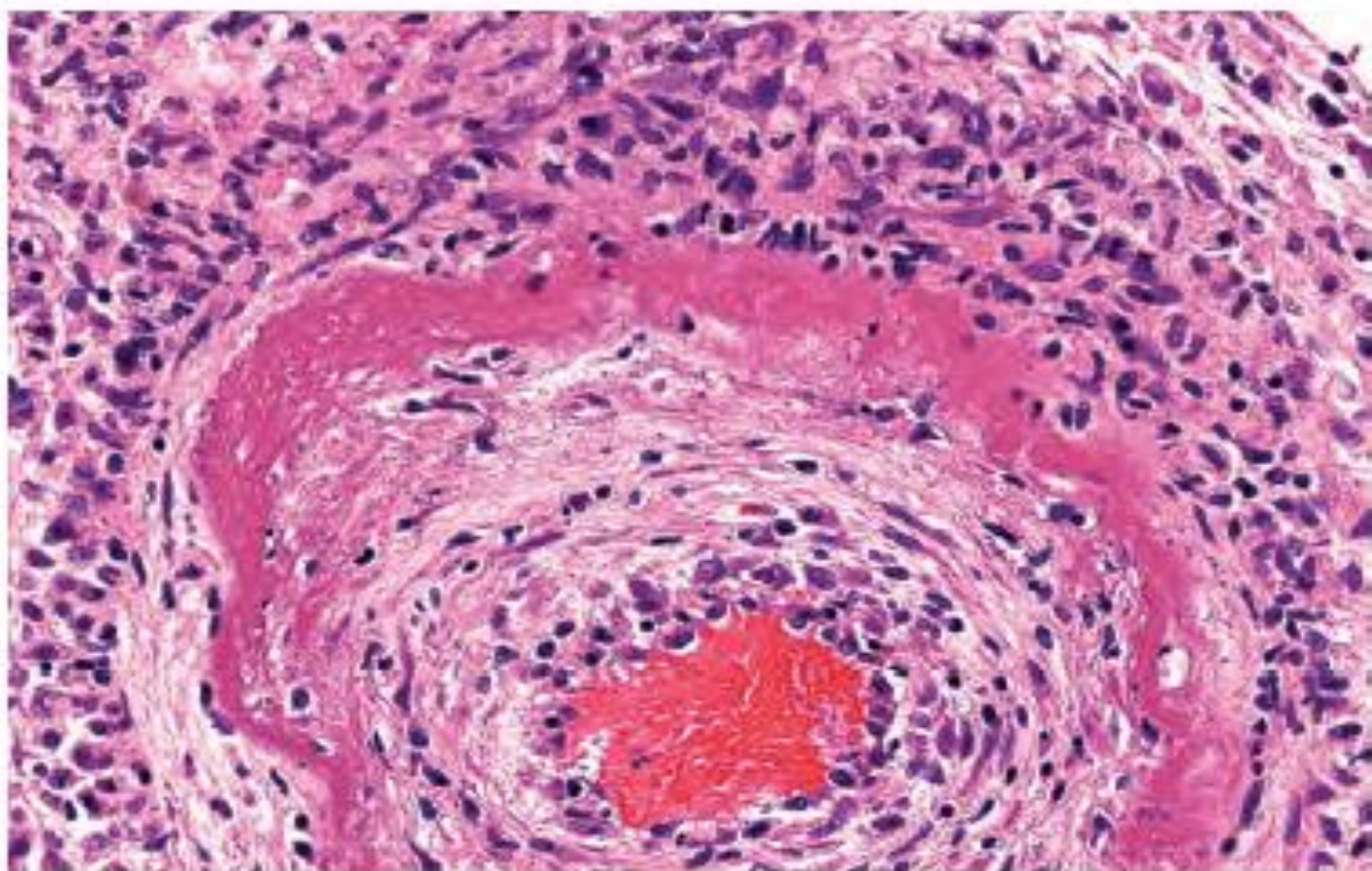
Cloudy appearance

Mixed inflammatory cells



H&E, X200





# POLLS

*Scan or Click to watch  
Cell Adaptation & Injury*



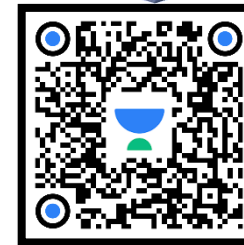
*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*





# **Necrosis with cell bodies retained as ghost cells is**

- a) Coagulative necrosis
- b) Liquefactive
- c) Caseous
- d) None

# Necrosis with cell bodies retained as ghost cells is

- a) Coagulative necrosis
- b) Liquefactive
- c) Caseous
- d) None

**All the following organs likely undergo coagulative necrosis except**

- a) Spleen
- b) Heart
- c) Kidney
- d) Brain

# **All the following organs likely undergo coagulative necrosis except**

- a) Spleen
- b) Heart
- c) Kidney
- d) Brain

# **Liquefactive necrosis is seen in -**

- a) Heart
- b) Brain
- c) Lungs
- d) Spleen

# **Liquefactive necrosis is seen in -**

- a) Heart
- **b) Brain**
- c) Lungs
- d) Spleen

**Thank you for being awake**



**THANK YOU**



# **GANGRENE**

# Headings

- Definition

- Types—>

- a) Introduction

- b) Gross

- c) Microscopy

# DEFINITION

- Gangrene is **necrosis of tissue associated with superadded putrefaction**

- **GANGRENE = Necrosis + Putrefaction**

# Headings

- Definition

- Types—>

- a) Introduction

- b) Gross

- c) Microscopy

# TYPES

2 main types of gangrene—

1. Dry

2. Wet

3. A variant of wet gangrene called **gas gangrene**.

1. **“Dry” gangrene** – **no bacterial superinfection**; tissue appears dry

2. **“Wet” gangrene** – **bacterial superinfection** has occurred; tissue looks wet and liquefactive

- In all types of gangrene, necrosis undergoes liquefaction by the action of putrefactive bacteria.

# Headings

- Definition

- Types—>

- a) Introduction

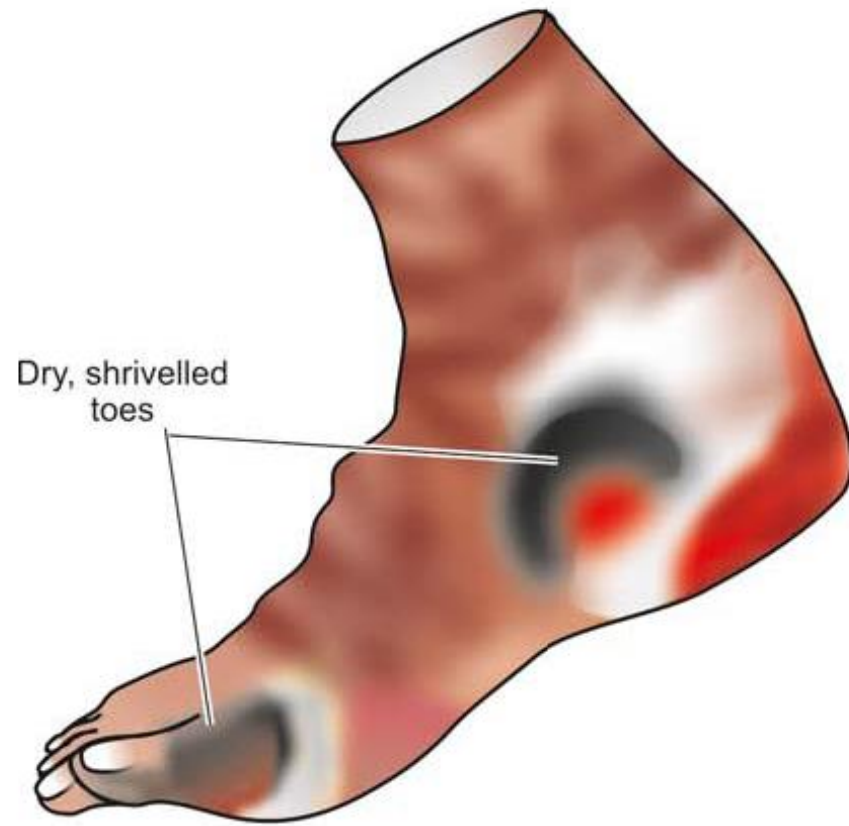
- b) Gross

- c) Microscopy



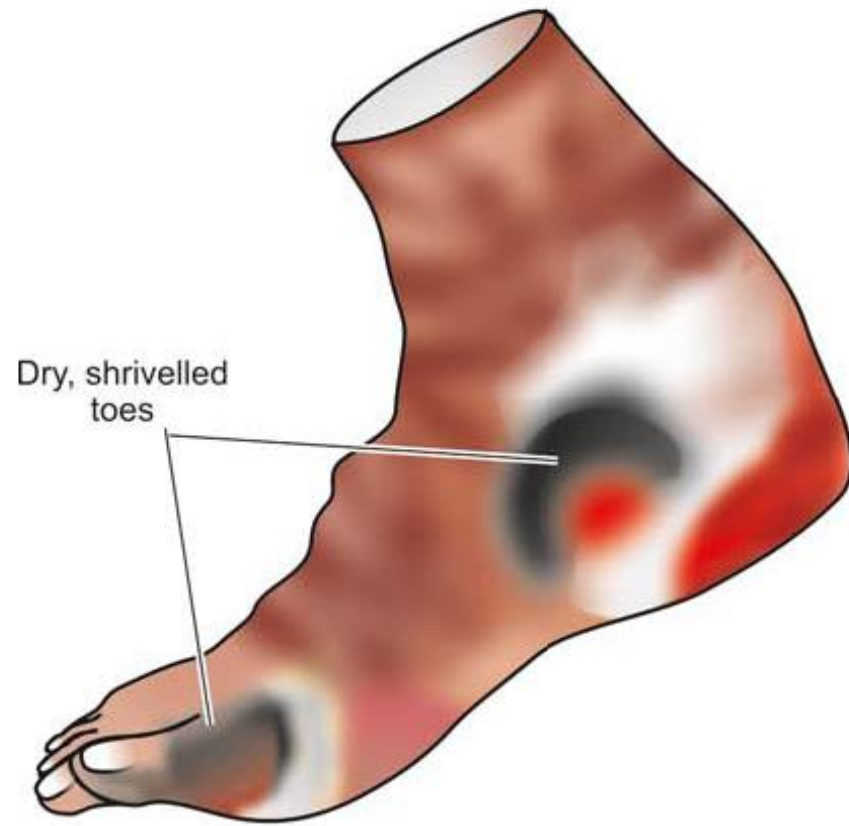
# Dry Gangrene

- Begins in the **distal part of a limb (toes ,feet)**
- Due to **ischaemia** ( blockage of **artery**).
- spreads **slowly** upwards until where the blood supply is adequate to keep the tissue viable.
- A **line of separation** is formed at this point between the gangrenous part and the viable part



**Figure 2.29** Dry gangrene of the foot. The gangrenous area is dry, shrunken and dark and is separated from the viable tissue by clear line of separation.

- It is a type of **coagulative necrosis**
- The extent of vascular occlusion is frequently global in the lower limbs, which impedes or prevents the migration of leukocytes in to the area of coagulative necrosis
- It is called gangrenous necrosis because **the dead tissue is not digested and removed but remains mummified.**



**Figure 2.29** Dry gangrene of the foot. The gangrenous area is dry, shrunken and dark and is separated from the viable tissue by clear line of separation.

# Headings

- Definition

- Types—>

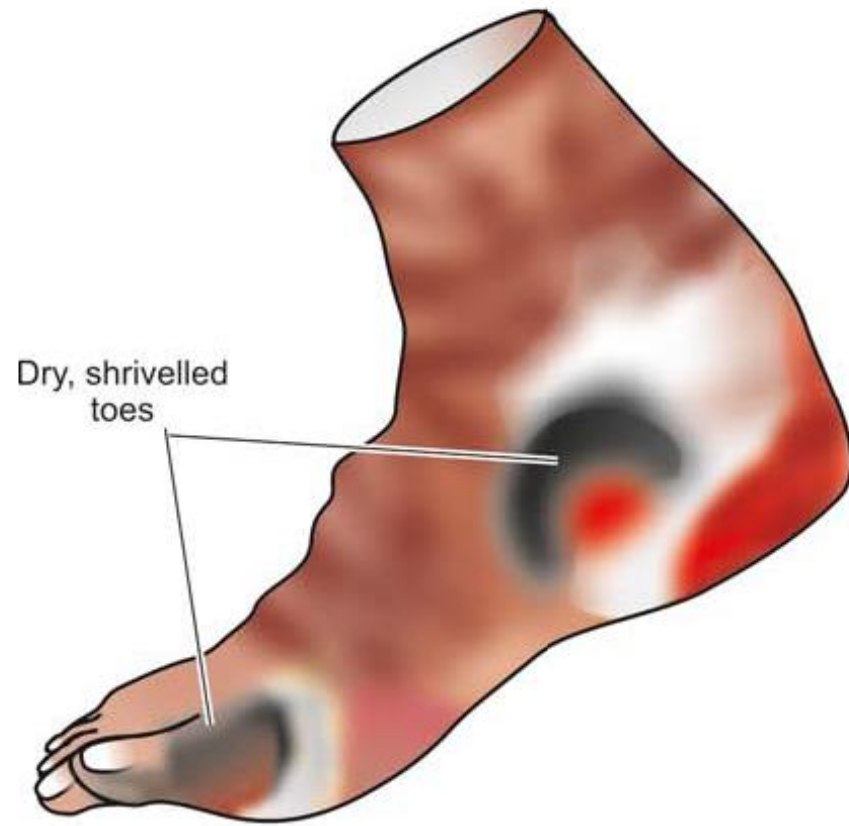
- a) Introduction

- b) Gross

- c) Microscopy

# Grossly

- Affected part is **dry, shrunken and dark black, resembling the foot of a mummy.**
- It is **black** due to liberation of haemoglobin from haemolysed red blood cells which is acted upon by hydrogen disulfide ( $H_2S$ ) produced by bacteria resulting in formation of black iron sulfide.
- **Line of separation**



**Figure 2.29** Dry gangrene of the foot. The gangrenous area is dry, shrunken and dark and is separated from the viable tissue by clear line of separation.



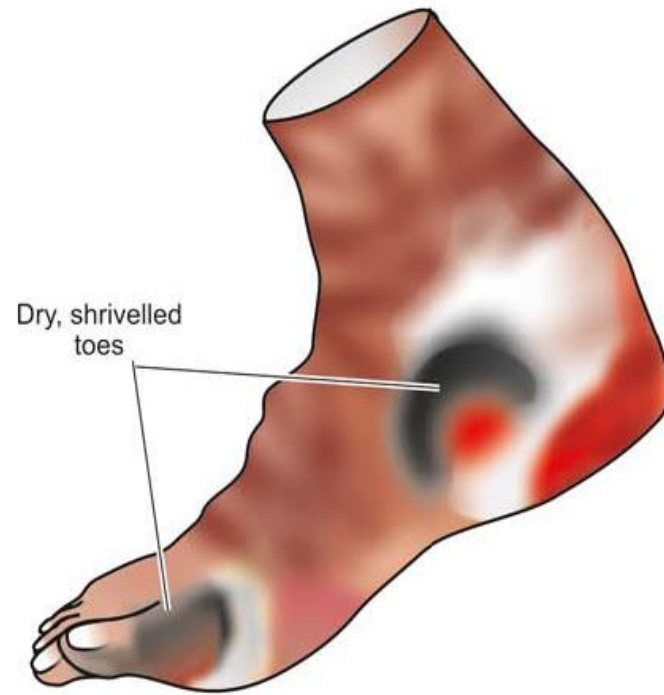




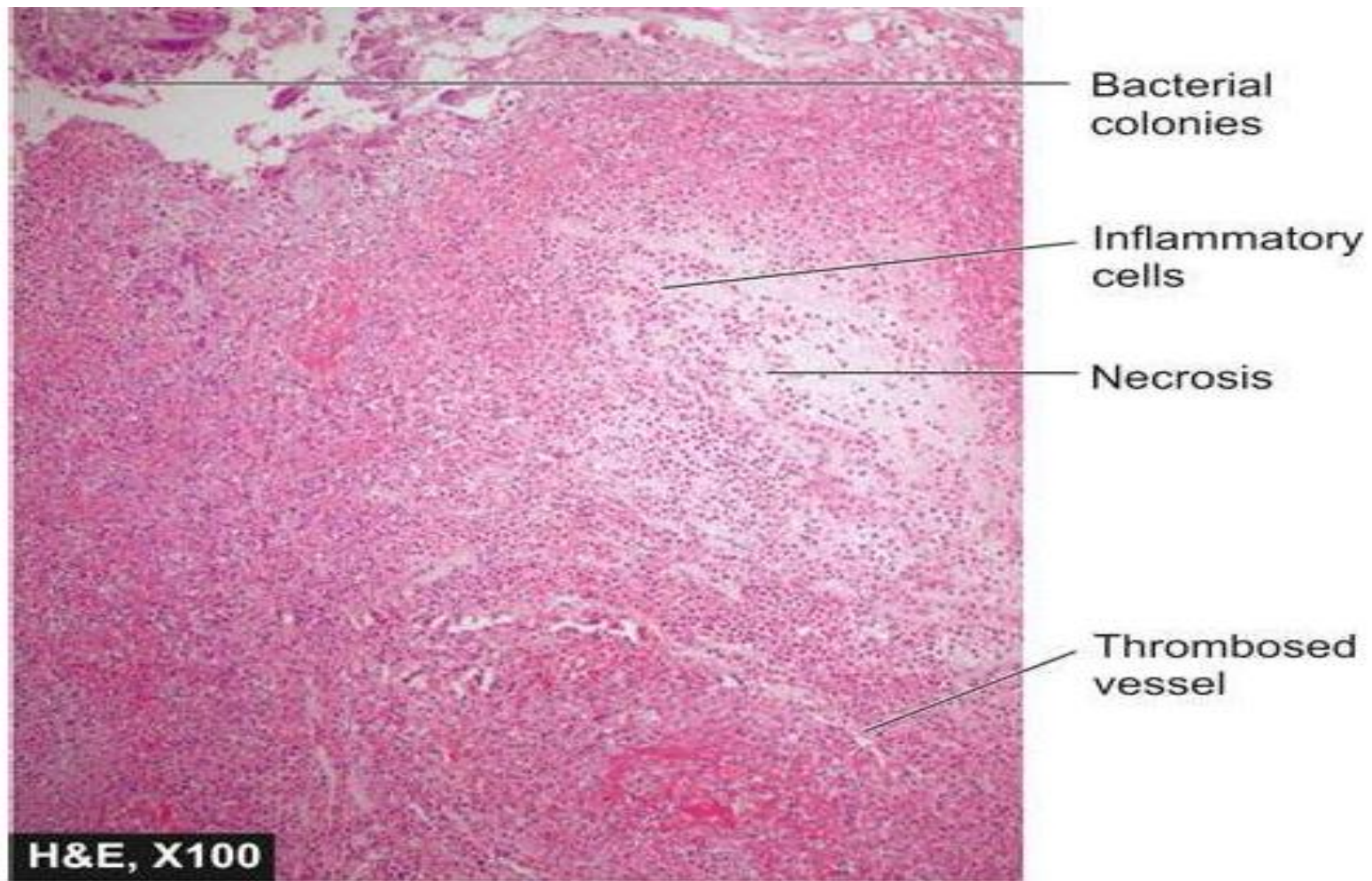


# **Histologically**

- There is coagulative necrosis with smudging of the tissue.
- Line of separation consists of inflammatory granulation tissue



**Figure 2.29** Dry gangrene of the foot. The gangrenous area is dry, shrunken and dark and is separated from the viable tissue by clear line of separation.



**Figure 2.30** Dry gangrene of the foot. Microscopy shows coagulative necrosis of the skin, muscle and other soft tissue, and thrombosed vessels.

# Headings

- Definition

- Types—>

- a) Introduction

- b) Gross

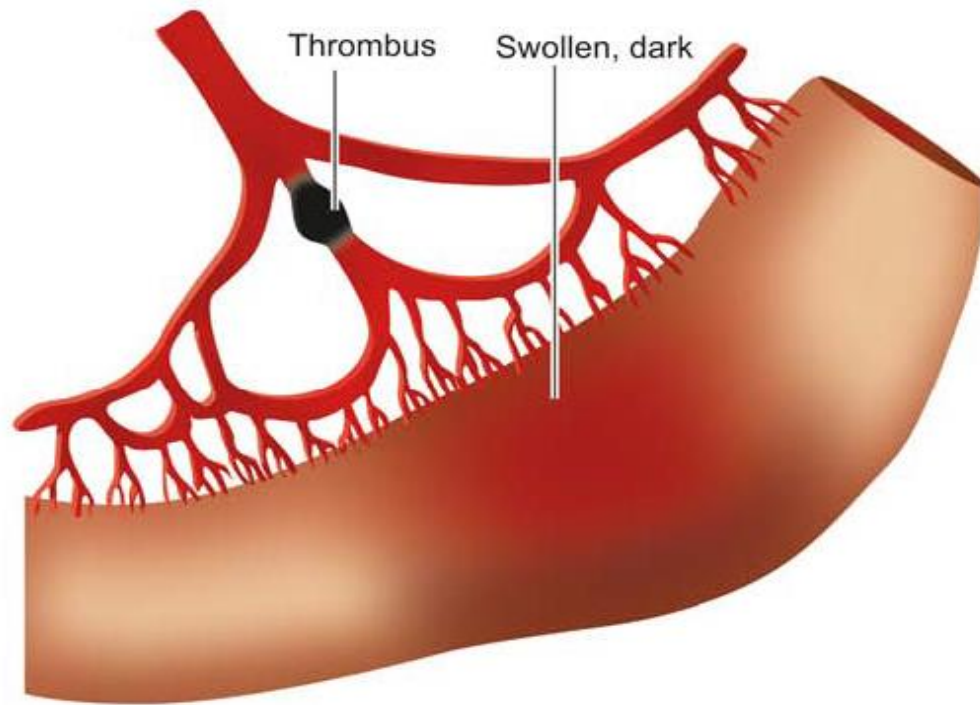
- c) Microscopy

# Wet Gangrene

- When overlying skin of dry gangrenous tissue is devitalized, **bacterial infection is superimposed**
- The coagulative necrosis is modified by **liquifactive necrosis.**

- Occurs in naturally **moist tissues and organs** such as the bowel, lung, mouth, cervix, vulva
- Develops due to blockage of **both venous as well as arterial blood flow**
- More **rapid.**
- **NO clear-cut line of demarcation**





**Figure 2.31** Wet gangrene of the small bowel. The affected part is soft, swollen and dark. Line of demarcation between gangrenous segment and the viable bowel is not clear-cut.





- The classic example is **gangrene of the bowel, commonly due to strangulated hernia.**
- **Diabetic foot** which is due to high glucose content favours growth of bacteria.

# Headings

- Definition

- Types—>

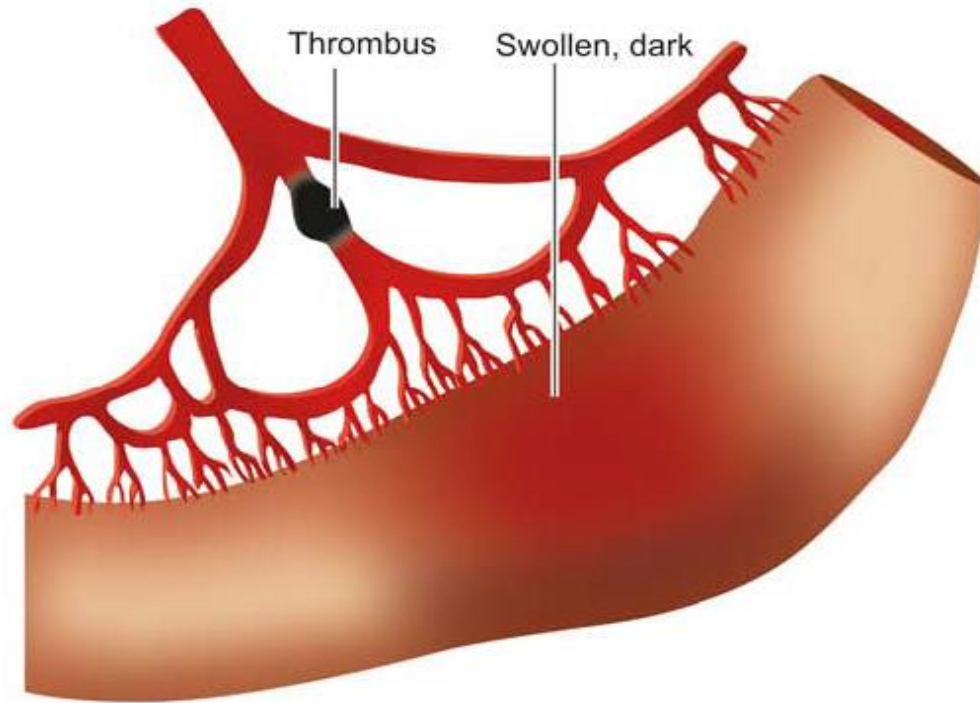
- a) Introduction

- b) Gross

- c) Microscopy

# Grossly

the affected part is **soft, swollen, putrid, rotten and dark.**



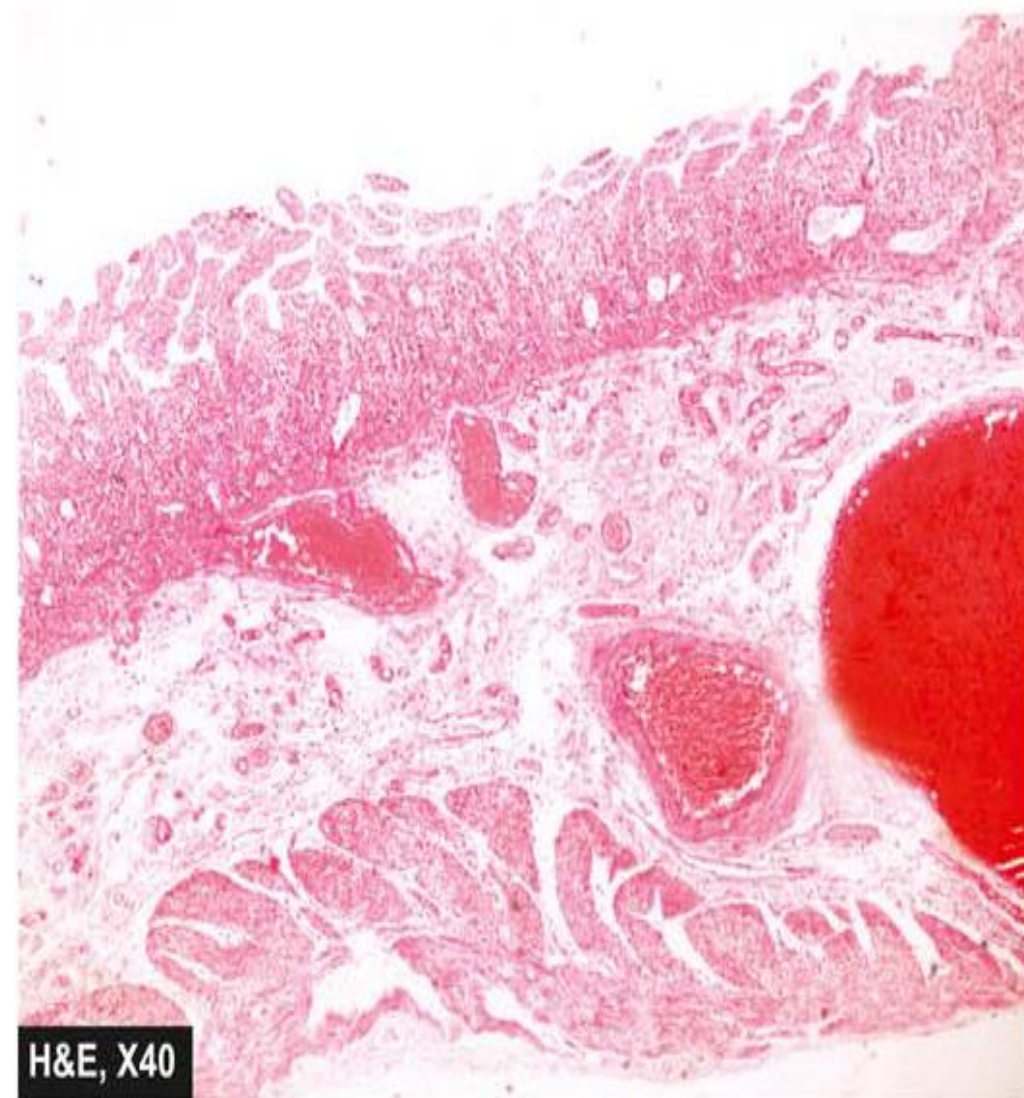
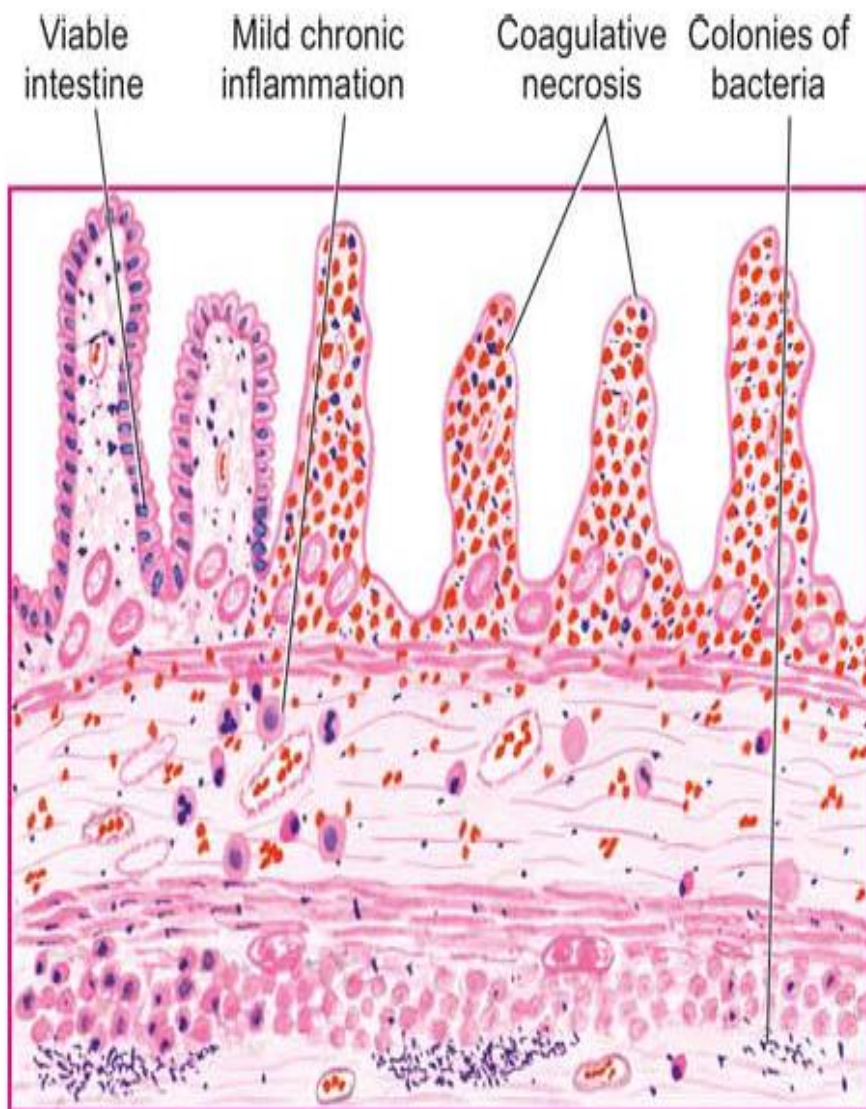
**Figure 2.31** Wet gangrene of the small bowel. The affected part is soft, swollen and dark. Line of demarcation between gangrenous segment and the viable bowel is not clear-cut.



# **Histologically**

- There is coagulative necrosis
- Mucosa is ulcerated and sloughed.
- Intense acute inflammatory exudates and
- Thrombosed vessel





**Figure 2.32** Wet gangrene of the small bowel. Microscopy shows coagulative necrosis of the affected bowel wall and thrombosed vessels while the junction with normal intestine is indistinct and shows an inflammatory infiltrate.

FEATURE	DRY GANGRENE	WET GANGRENE
1. <i>Site</i>	Commonly limbs	More common in bowel
2. <i>Mechanisms</i>	Arterial occlusion	Blockage of both venous drainage and arterial obstruction
3. <i>Macroscopy</i>	Organ dry, shrunken and black	Part moist, soft, swollen, rotten and dark
4. <i>Putrefaction</i>	Limited due to very little blood supply	Marked due to stuffing of organ with blood
5. <i>Line of demarcation</i>	Present at the junction between healthy and gangrenous part	No clear line of demarcation
6. <i>Bacteria</i>	Bacteria fail to survive	Numerous present
7. <i>Prognosis</i>	Generally better due to little septicaemia	Generally poor due to profound toxemia

# REMEMBER

- Dry gangrene -> Variant of Coagulative necrosis
- Wet gangrene -> Liquifactive necrosis is superimposed on coagulative necrosis



# Headings

- Definition
- Types—>
  - a) Introduction
  - b) Gross
  - c) Microscopy

# **GAS GANGRENE**

- Special form of wet gangrene caused by **gas-forming clostridia (gram-positive anaerobic bacteria)**
- It enters through open contaminated wounds or complication of operation on colon which normally contains clostridia.

# Headings

- Definition

- Types—>

- a) Introduction

- b) Gross

- c) Microscopy

# Grossly

- **Swollen, oedematous, painful and crepitant** due to accumulation of gas bubbles of carbon dioxide within the tissues formed by fermentation of sugars by bacterial toxins





# **Microscopically**

- Coagulative necrosis with liquefaction.
- Large number of gram-positive bacilli can be identified.
- leucocytic infiltration, oedema
- Capillary and venous thrombi are common.

QUESTIONS???



**All are cellular adaptations except -**

- a) Hypertrophy
- b) Hyperplasia
- c) Necrosis
- d) Metaplasia

*(All India Dec.13 Pattern)*

C

**Example of physiological atrophy is?**

- a) Senile atrophy *(CET July 16 Pattern)*
- b) Disuse atrophy
- c) Post pregnancy uterine atrophy
- d) All of the above

C

**Both hyperplasia and hypertrophy is found in-**

- a) Pregnancy uterus *(AIIMS May 09)*
- b) Cardiac muscle in cardiomegaly
- c) Skeletal muscle in athlete
- d) Breast development in puberty

A

**Cellular swelling with blebs and myelin figures are  
the changes seen in -** *(All India Dec.15 Pattern)*

- a) Reversible cell injury
- b) Irreversible cell injury
- c) Metaplasia
- d) Anaplasia

A



**Not an irreversible injury?**

*(NEET Dec 16 Pattern)*

- a) Pyknosis
- b) Karyorrhexis
- c) Karyolysis
- d) Bleb formation

D

**Irreversible cell injury-**

*(NEET Dec.12 Pattern)*

- a) Mitochondrial densities
- b) Cellular swelling
- c) Blebs
- d) None

A

**Which of the following is not a free radical scavenger-**

*(All India Dec.15 Pattern)*

- a) Glutathione peroxidase
- b) Superoxide dismutase
- c) Catalase
- d) Xanthine oxidase

D

**Spread of infection causes -**

- a) Fibrinoid necrosis
- b) Fat necrosis
- c) Liquifactive necrosis
- d) Coagulative necrosis

C



**All the following organs likely undergo coagulative  
necrosis except -** *(All India Dec.15 Pattern)*

- a) Spleen
- b) Heart
- c) Kidney
- d) Brain

D

**MI is a type of -**

*(NEET Dec 16 Pattern)*

- a) Coagulative necrosis
- b) Liquefactive necrosis
- c) Caseous necrosis
- d) Fat necrosis

A

## **Type of necrosis occurring in brain -**

a) Coagulative

*(All India Dec.13 Pattern)*

b) Liquefactive

c) Fibrinoid

d) Caseous

B

**Coagulative necrosis is seen in A/E -**

*(AIIMS May 95, AI 97)*

- a) M.I.
- b) T.B.
- c) Thermal
- d) Zenker's degeneration

B



## **Type of necrosis in pancreatitis-**

*(All India Dec.13 Pattern)*

- a) Fibrinoid
- b) Coagulative
- c) Fat
- d) Caseous

C

**Trauma to breast causes which type of necrosis -**

a) Coagulative necrosis

*(All India Dec.15 Pattern)*

b) Liquefactive necrosis

c) Caseous necrosis

d) Fat necrosis

D

**The earliest change seen in apoptosis is -**

- a) Cell shrinkage *(CET Nov.15 Pattern)*
- b) Pyknosis
- c) Formation of apoptotic bodies
- d) Fragmentation of cells

A

**Apoptosis is differentiated from necrosis by  
presence of following feature-** *(CET July 16 Pattern)*

- a) Absence of inflammation
- b) Cell swelling
- c) Disruption of plasma membrane
- d) Passive process

A



**True about Apoptosis are all except-**

- a) Inflammation is present *(NEET Dec 16 Patter)*
- b) Chromosomal brekage
- c) Clumping of chromatin
- d) Cell shrinkage

A

**All of the following are features of apoptosis, except-**

- a) Cellular swelling *(AI 10)*
- b) Nuclear compaction
- c) Intact cell membrane
- d) Cytoplasmic eosiophilia

A

**Which of the following organelles plays a pivotal role in apoptosis?**

*(AIIMS May 10, AI 11, 09)*

- a) Mitochondria
- b) Endoplasmic reticulum
- c) Nucleus
- d) Golgi apparatus

A

**CD 95 is a marker of -**

*(AIIMS Nov. 12)*

- a) Intrinsic pathway of apoptosis
- b) Extrinsic pathway of apoptosis
- c) Monocyte
- d) Leucocyte

B



**In apoptosis, cytochrome C acts through -**

a) Apaf 1

*(NEET Dec.12 Pattern)*

b) Bcl-2

c) FADD

d) TNF

A

**Execution caspases of apoptosis are -**

- a) Caspase 1 & 3
- b) Caspase 3 & 5
- c) Caspase 1 & 5
- d) Caspase 3 & 7

*(All India Dec.15 Pattern)*

D

**The following is an antiapoptotic gene -**

- a) Bax
- b) Bad
- c) Bcl-X
- d) Bim

*(AIIMS Nov 06)*

C

**Antiapoptotic protein among the following is?**

a) MCL-1

*(NEET Dec 16 Pattern)*

b) P53

c) BAX

d) BIM

A



**Annexin V is a marker of-**

*(NEET Dec.12 Pattern, AIIMS May 09)*

- a) Apoptosis
- b) Necrosis
- c) Artherosclerosis
- d) Inflammation

A

## **Liquefactive action on necrotic tissue results**

**in -**

*(All India Dec.13 Pattern)*

- a) Gangrene
- b) Embolism
- c) Infarct
- d) Caseation

A

**Infected gangrene of skin and subcutaneous tissues  
is?**

*(CET July 16 Pattern)*

- a) Dry gangrene
- b) Wet gangrene
- c) Erysipelas
- d) None of the above

B

**Diabetic foot is associated with following type of gangrene?**

*(NEET Dec 16 Pattern)*

- a) Dry gangrene
- b) Wet gangrene
- c) Gas gangrene
- d) Fournier's gangrene

B



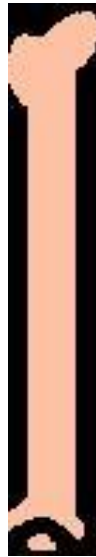


**Thank You**

# **Pathological calcification**

# CALCIUM

**Insoluble inorganic calcium salts are a normal constituent  
of **bones and teeth.****



# CALCIUM

- The great majority of the calcium in the body is stored in bone and teeth
- The bulk of remaining calcium is bound to protein or forms small ionic complexes.
- It is estimated that **1% or less of the calcium** in the body is present in ionic form, the active form of the element.

# CALCIUM

- Furthermore, the calcium concentration **outside of cells** is approximately 10,000 fold higher than inside cells.
- Within cells, calcium is 10,000 fold higher in the **endoplasmic reticulum and mitochondria** than in the cytosol.

# **CALCIUM HOMEOSTASIS**

- **Vitamin D (1,25-dihydroxycholecalciferol)**
- **Parathormone**
- **Calcitonin**

# **Vitamin D (1,25-dihydroxycholecalciferol):**

## **Stimulus**

- Low extracellular calcium
- Parathormone stimulates formation of 1,25-dihydroxycloecalciferol by the kidney

## **Main Action** – lead to increased extracellular calcium

- increase the absorption of calcium and phosphorus from the intestine.

# Parathormone

## Stimulus

- Low extracellular calcium
- Elevated extracellular phosphorus

## Main actions – lead to increased extracellular calcium

- Stimulates formation of vitamin D by the kidney
- Increased mobilization of calcium from bone
- Increasing absorption of calcium from the intestine
- Promotes resorption of calcium from the kidney
- Promotes excretion of phosphorus in the urine



# Calcitonin

## Stimulus

- Elevated extracellular calcium

## Action – lowers extracellular calcium

- Inhibits the parathormone-induced release of calcium from bone
- Promotes the urinary excretion of phosphorus

# **PATHOLOGICAL CALCIFICATION**

- **Deposition of calcium salts in tissues other than osteoid or enamel is called pathologic or heterotopic calcification**
- **It is abnormal deposition of calcium salts, together with smaller amounts of iron, magnesium and mineral salts in cells and tissues that are not normally mineralized.**

# **TYPES**

**2 forms:**

**1. Dystrophic**

**2. Metastatic**

# **Dystrophic calcification:**

- Calcification of **dead and dying tissues**.
- The level of calcium in blood is usually normal. (There is **no hypercalcemia**).
- Calcification occurs in two phases- initiation and propagation

- within the cells or extra-cellularly
1. Extracellular initiation occurs in **small vesicles derived from degenerating cells**
  2. Initiation of intra-cellular calcification occurs in the **mitochondria** of dead or dying cells.

Membrane of dead and degenerated cell damaged,

Phospholipid is released

Phosphatases within the phospholipid generate phosphate ions

calcium binds to phosphate ions

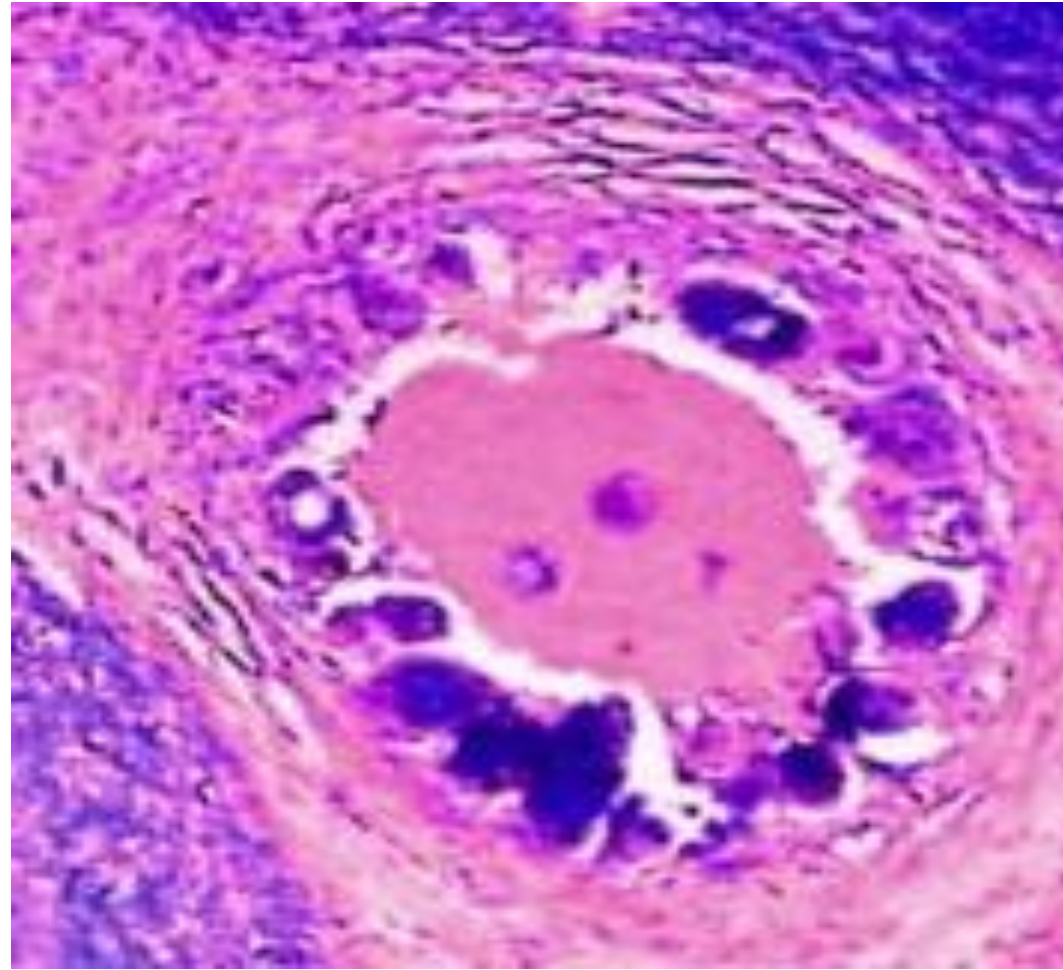
forming calcium phosphate



# Sites of calcification:

## Dead tissues

- caseation eg. Tuberculosis
- Dead parasites like trichinosis, Onchocercosis.
- fat necrosis
- infarcts
- thrombi
- haematoma

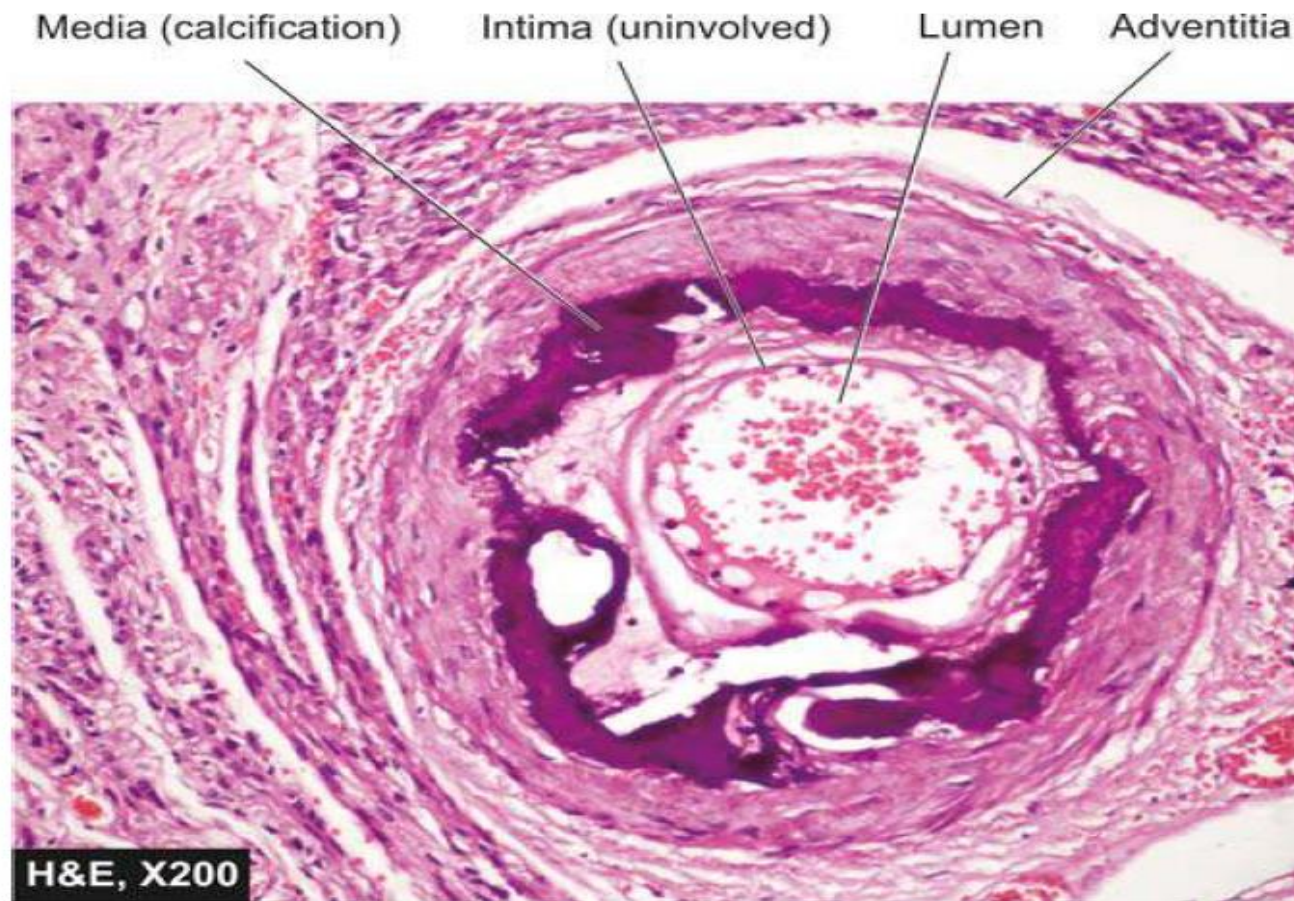




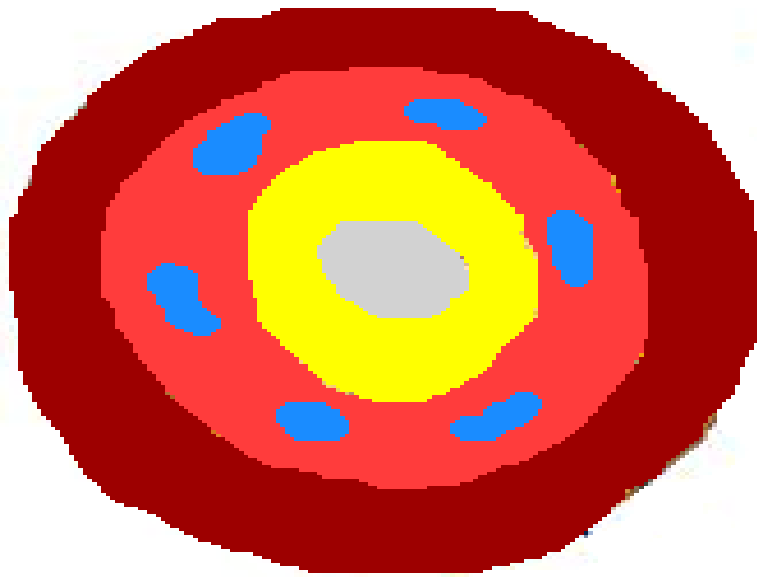
# Sites of calcification:

## Degenerative tissues

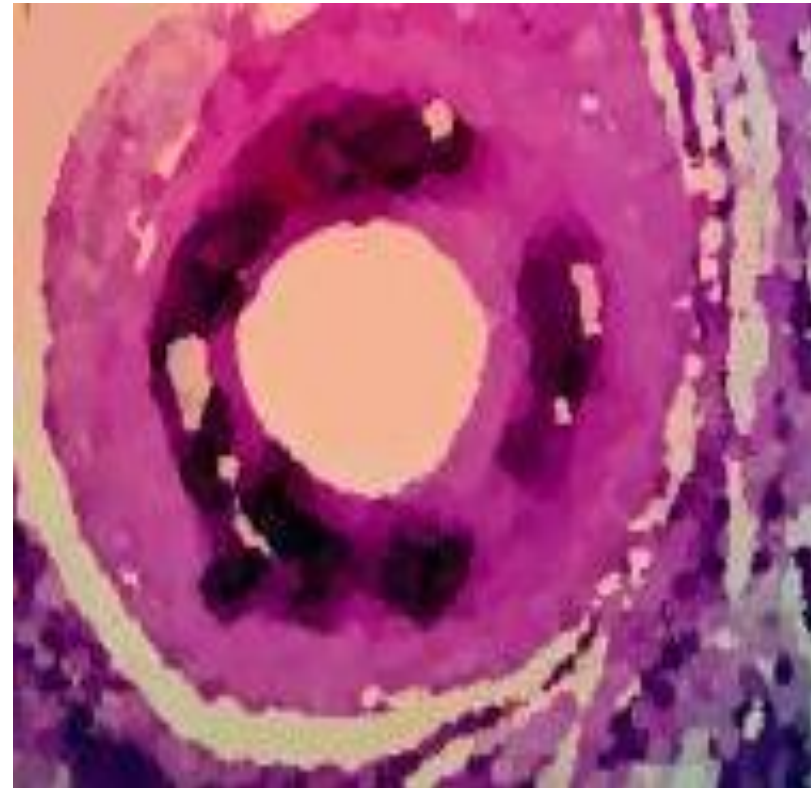
- – atherosclerosis- monckeberg sclerosis
- – damaged heart valves
- – infected lymph nodes
- – degenerating tumours



**Figure 2.34** Dystrophic calcification in degenerated tunica media of muscular artery of uterine myometrium in Mönckeberg's arteriosclerosis.



**Monckeberg's Sclerosis -  
Calcification of Tunica  
Media.**



### **Dystrophic calcification in dead tissues**

- In caseous necrosis of tuberculosis (**most common which may be in lymph nodes<sup>(NEET)</sup>**)
- Chronic abscess in liquifactive necrosis
- Fungal granuloma
- Infarct
- Thrombi
- Haematomas
- Dead parasites-Cystecercosis/Toxoplasma  
Hydatid/Schistosoma
- In fat necrosis of breast & other tissues

### **Dystrophic calcification in degenerated tissues**

- **Atheromatous plaque<sup>(AI 13)</sup>**
- Monkeberg's sclerosis
- **Psommama bodies<sup>(DNB 08)</sup>**
- Dens old scars
- Senile degenerated changes such as in costal cartilage, tracheal, bronchial rings, Pineal gland in brain.
- **Heart valves damaged by rheumatic fever<sup>(NEET)</sup>.**

# **TYPES**

**2 forms:**

**1. Dystrophic**

**2. Metastatic**

# Metastatic calcification

It is deposition of calcium salts in many **tissues which may be normal.**

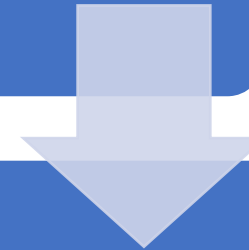
It is associated with disorders of calcium metabolism and there is **hypercalcemia.**

It may occur widely throughout the body, hence the term “metastatic.”

Those organs that 'lose' acid



Have an underlying alkaline compartment.



An alkaline internal component is susceptible to calcification.

# Sites of calcification:

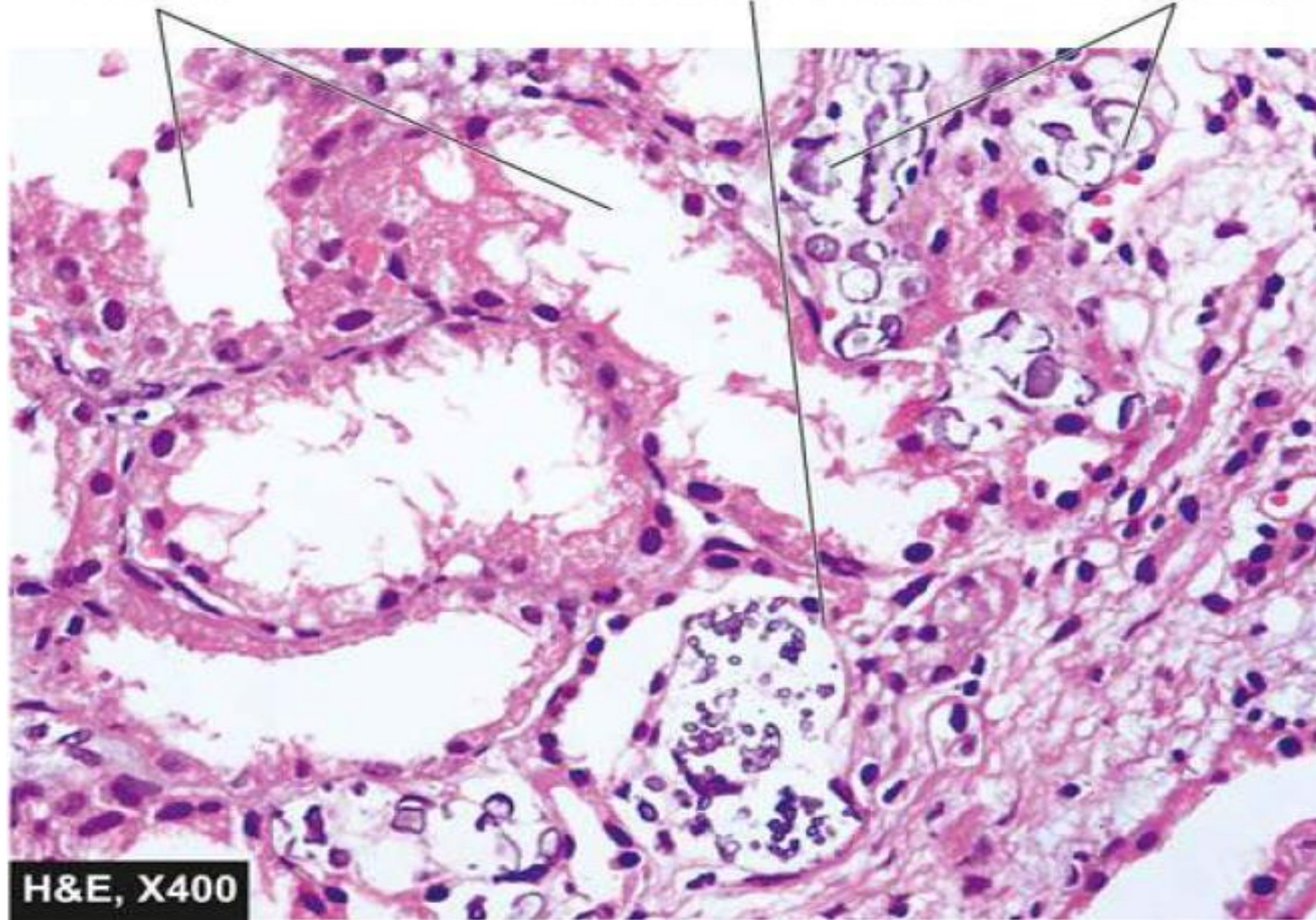
- Basement membrane & tubular lamina of kidney<sup>(NEET, AIIMS 05)</sup>
- Pulmonary veins
- Alveolar wall of lung (most common site)<sup>(NEET, AIIMS 05)</sup>
- Cornea & Conjunctiva
- Interstitial tissue of gastric mucosa<sup>(AIIMS 05)</sup>
- Synovium of the joint
- Systemic arteries
- Tendons.



Tubules

Basement membrane

Calcification



H&E, X400

# **Causes:**

1. **Hyperparathyroidism-** A. Primary, due to neoplasm  
B. Secondary-nutritional or renal failure (uremia)
2. **Hypervitaminosis-D** (Vit.D Toxicosis). Increased absorption of Ca from intestine.
3. **Neoplasms:** Lymphosarcoma and apocrine adenocarcinoma secrete parathyroid hormone-like peptides and cause hypercalcemia.

# **TYPES**

**2 forms:**

**1. Dystrophic**

**2. Metastatic**

- **Gross and microscopic appearance is similar to dystrophic and metastatic calcification.**

# Gross

- Calcification appears as **pale chalky white** areas in the tissues.
- Even if not visible, calcification can sometimes be detected by the **coarse gritty feel** of the tissues when scraped or incised with a knife or scalpel blade.





1044 2008

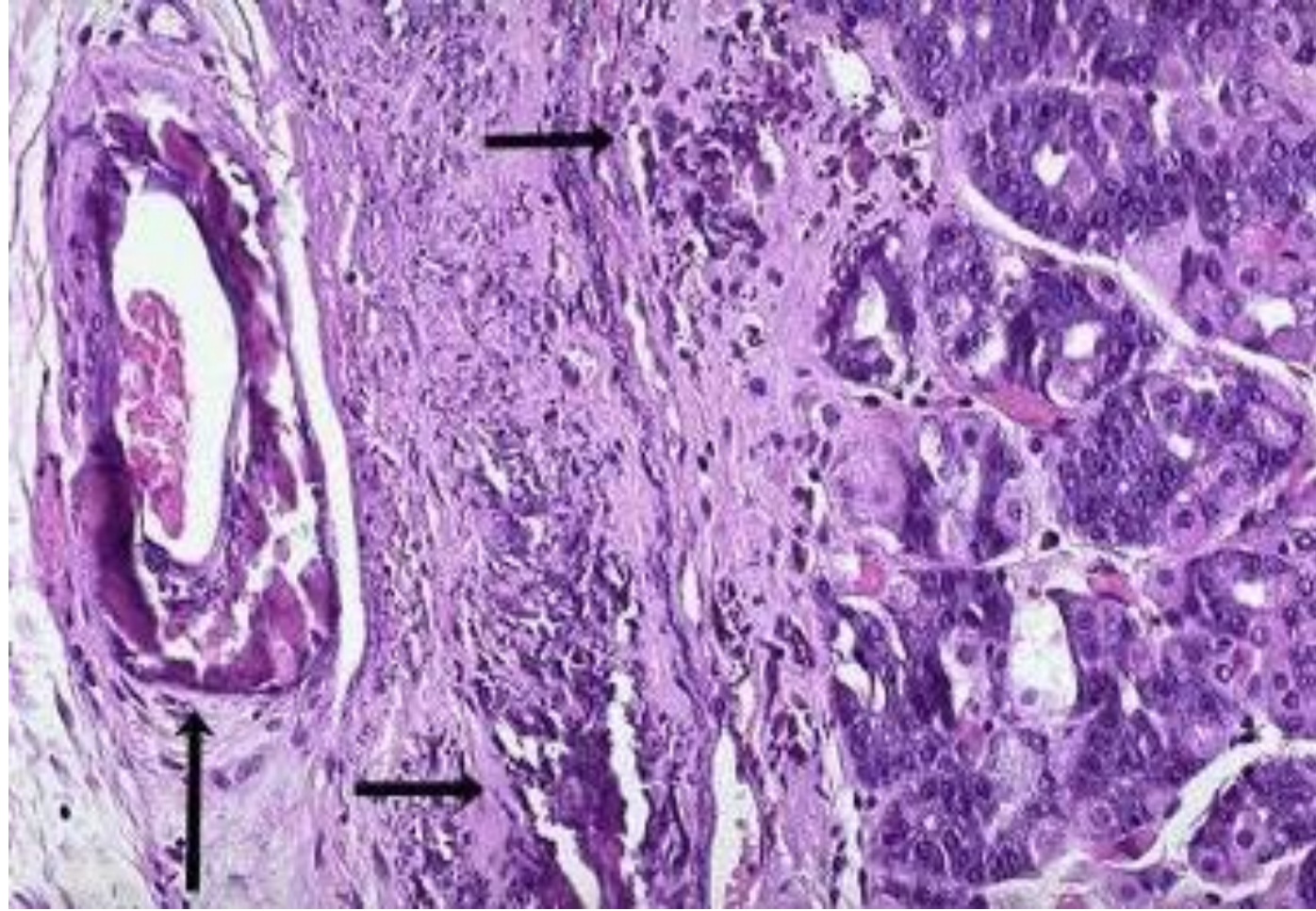


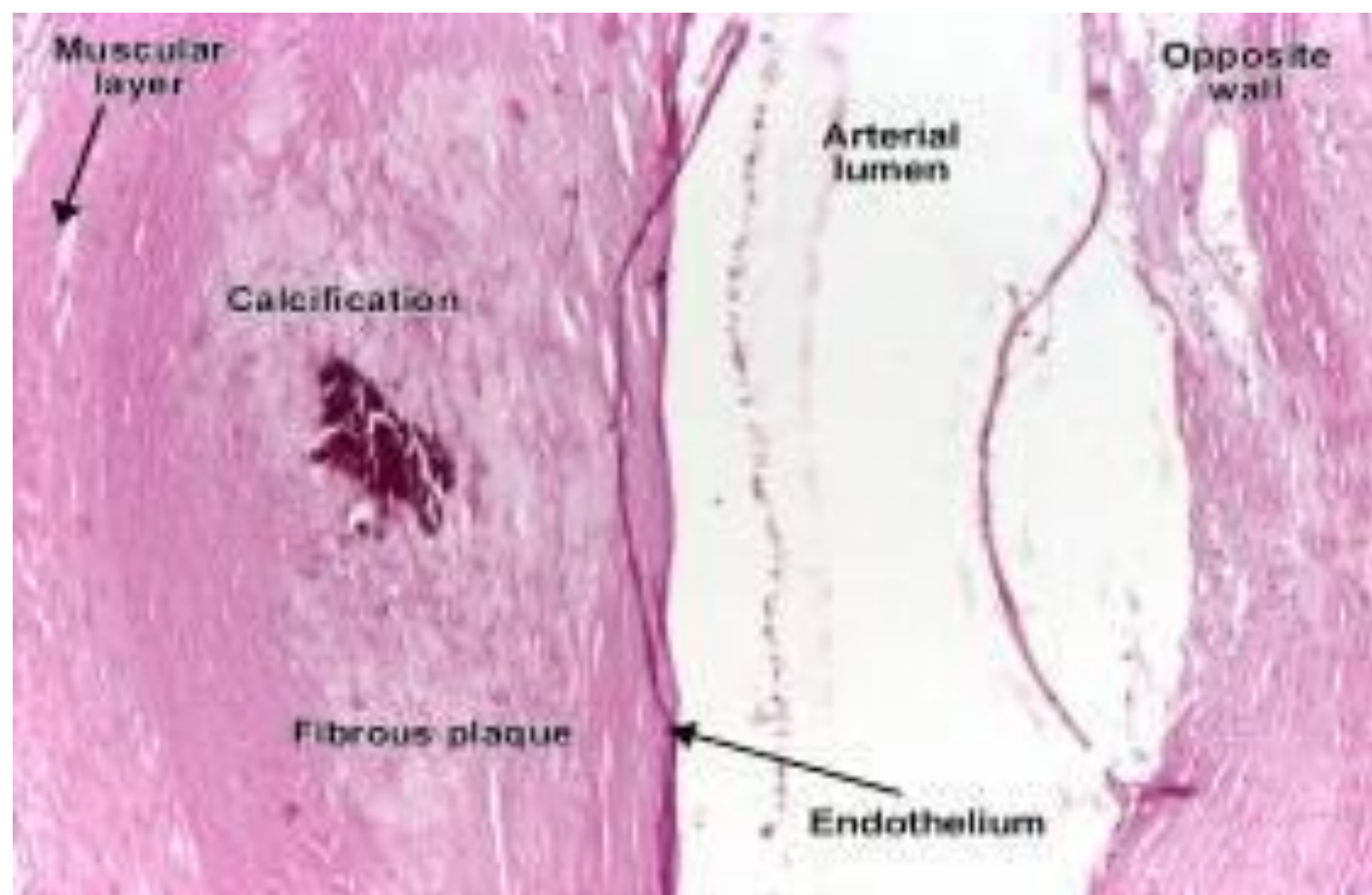


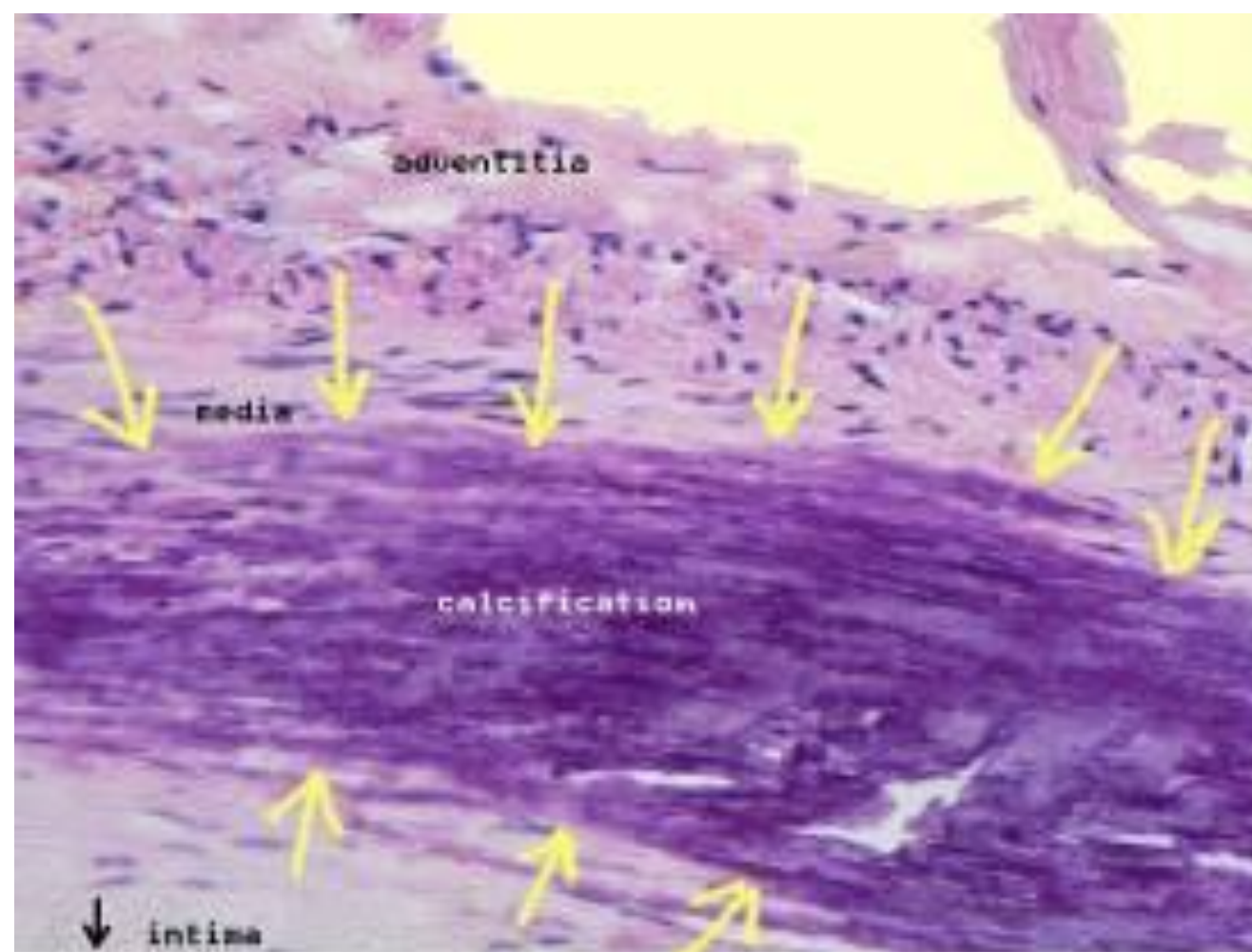


# Microscopic appearance:

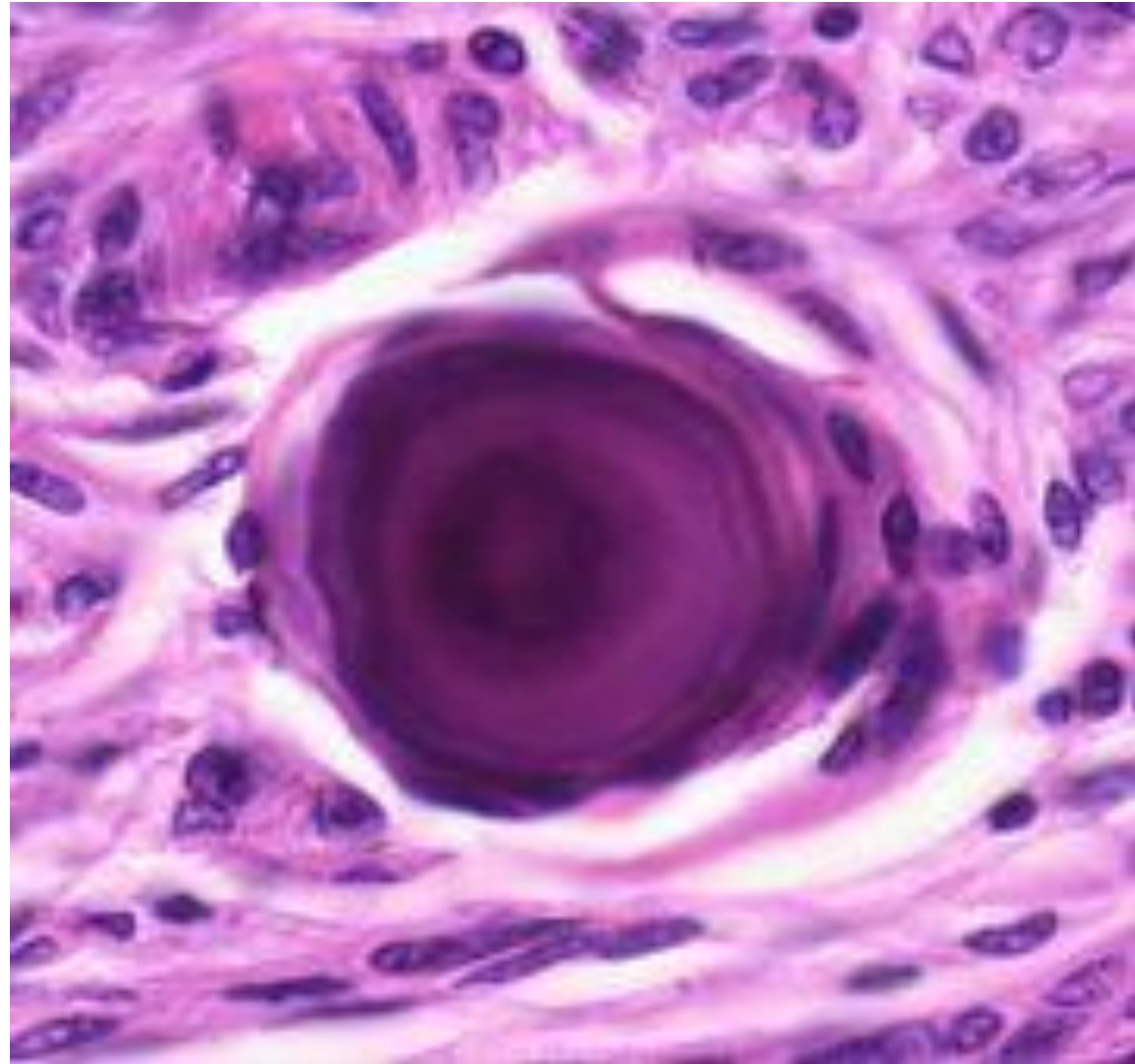
- Calcium salts appear as **blue granules (deep basophilic) on H& E.**
- Single necrotic cells act like little grains of sand around which a “pearl” of calcium is deposited. This is called a **psammoma body**
- Special stain **Von Kossa** gives a **black** color, ***Alizarin red S*** that produces **red** staining











# Significance and results

- Calcification is usually **harmless**.
- May cause hindrance to organs motility and **inelasticity**.

Both types of calcification consist of **calcium phosphate crystals**.

The big difference is that →

- **Dystrophic calcification** occurs in damaged tissue and normal blood calcium level
- **Metastatic calcification** occurs in normal tissue in the setting of hypercalcemia

FEATURE	DYSTROPHIC CALCIFICATION	METASTATIC CALCIFICATION
1. <i>Definition</i>	Deposits of calcium salts in dead and degenerated tissues	Deposits of calcium salts in normal tissues
2. <i>Calcium metabolism</i>	Normal	Deranged
3. <i>Serum calcium level</i>	Normal	Hypercalcaemia
4. <i>Reversibility</i>	Generally irreversible	Reversible upon correction of metabolic disorder



5. <i>Causes</i>	Necrosis (caseous, liquefactive, fat), infarcts, thrombi, haematomas, dead parasites, old scars, atheromas, Mönckeberg's sclerosis, certain tumours, cysts, calcinosis cutis	Hyperparathyroidism (due to adenoma, hyperplasia, carcinoma), chronic renal failure (CRF), bony destructive lesions (e.g. myeloma, metastatic carcinoma), prolonged immobilisation, hypervitaminosis D, milk-alkali syndrome, hypercalcaemia of infancy
6. <i>Pathogenesis</i>	Increased binding of phosphates with necrotic and degenerative tissue, which in turn binds to calcium forming calcium phosphate precipitates	Increased precipitates of calcium phosphate due to hypercalcaemia at certain sites e.g. in lungs, stomach, blood vessels and cornea

# DYSTROPHIC

NORMAL SERUM CALCIUM  
DEAD & DYING TISSUES

ATHEROSCLEROSIS

CALCIFIED GRANULOMAS

CALCIFIC AORTIC STENOSIS

BICUSPID AORTIC STENOSIS

## EXTRASKELETAL CALCIFICATION

# METASTATIC

**HYPERCALCEMIC STATES**  
CALCIFICATION IN NORMAL  
TISSUES: LUNG, KIDNEY,  
GASTRIC MUCOSA

**MULTIPLE MYELOMA**  
**HYPERPARATHYROIDISM**  
**BONE METASTASIS**  
**END-STAGE KIDNEY**  
**SARCOIDOSIS**  
**HYPERVITAMINOSIS D**

**AGING**

- Cellular aging is the result of a **progressive decline in cellular function and viability** caused by **genetic abnormalities and the accumulation of cellular damage due to the effects of exposure to exogenous influences**
- Ageing is distinct from mortality and disease although aged individuals are more vulnerable to disease.

- In India, due to improved health care, it has gone up from an average of 26 years at the time of independence in 1947 to 64 years at present.
- Survival is longer in **women than men (3: 2)**.
- The maximum human lifespan has remained stable at about **110 years**.

# Life expectancy of an individual depends on

## 1. Intrinsic genetic process

- the genes controlling response to endogenous and exogenous factors.
- It has been seen that long life runs in families
- high concordance in lifespan of identical twins has been observed.

## 2. Environmental factors

**3. Lifestyle of the individual** such as diseases due to alcohol, smoking, drug addiction.

**4. Age-related diseases** e.g. atherosclerosis and IHD, DM, hypertension, osteoporosis, Alzheimer's disease, Parkinson's disease etc.

# **PATHOGENESIS OF AGING**

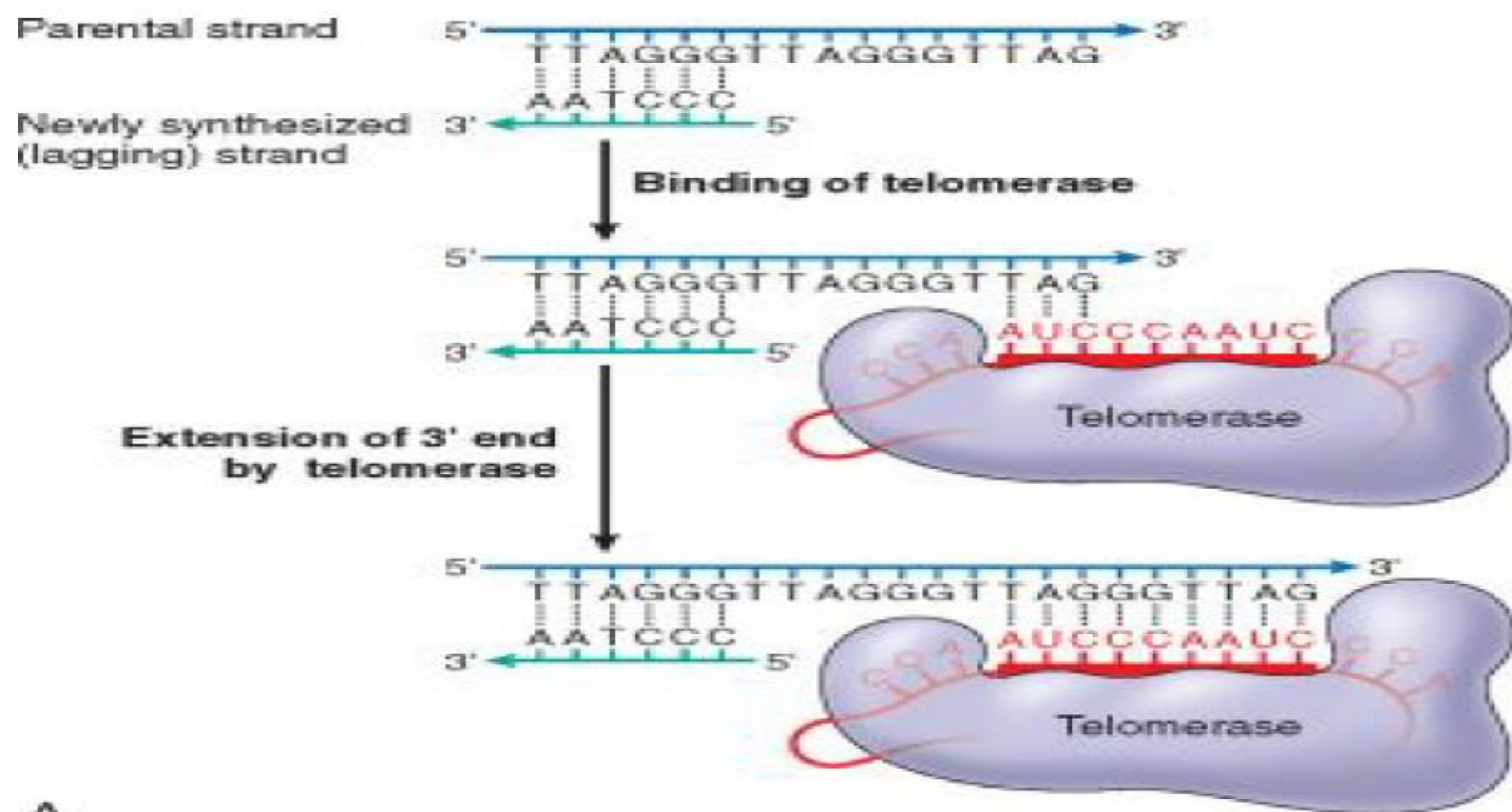
- **1. TELOMERE THEORY**
- **2. Genetic control in invertebrates**
- **3. Diseases of accelerated ageing**
- **4. Oxidative stress hypothesis (free radical-mediated injury)**
- **5. Hormonal decline**
- **6. Defective host defenses**
- **7. Failure to renew**

# 1. TELOMERE THEORY

- After a fixed number of divisions all somatic cells become arrested in a terminally nondividing state, known as **senescence**.

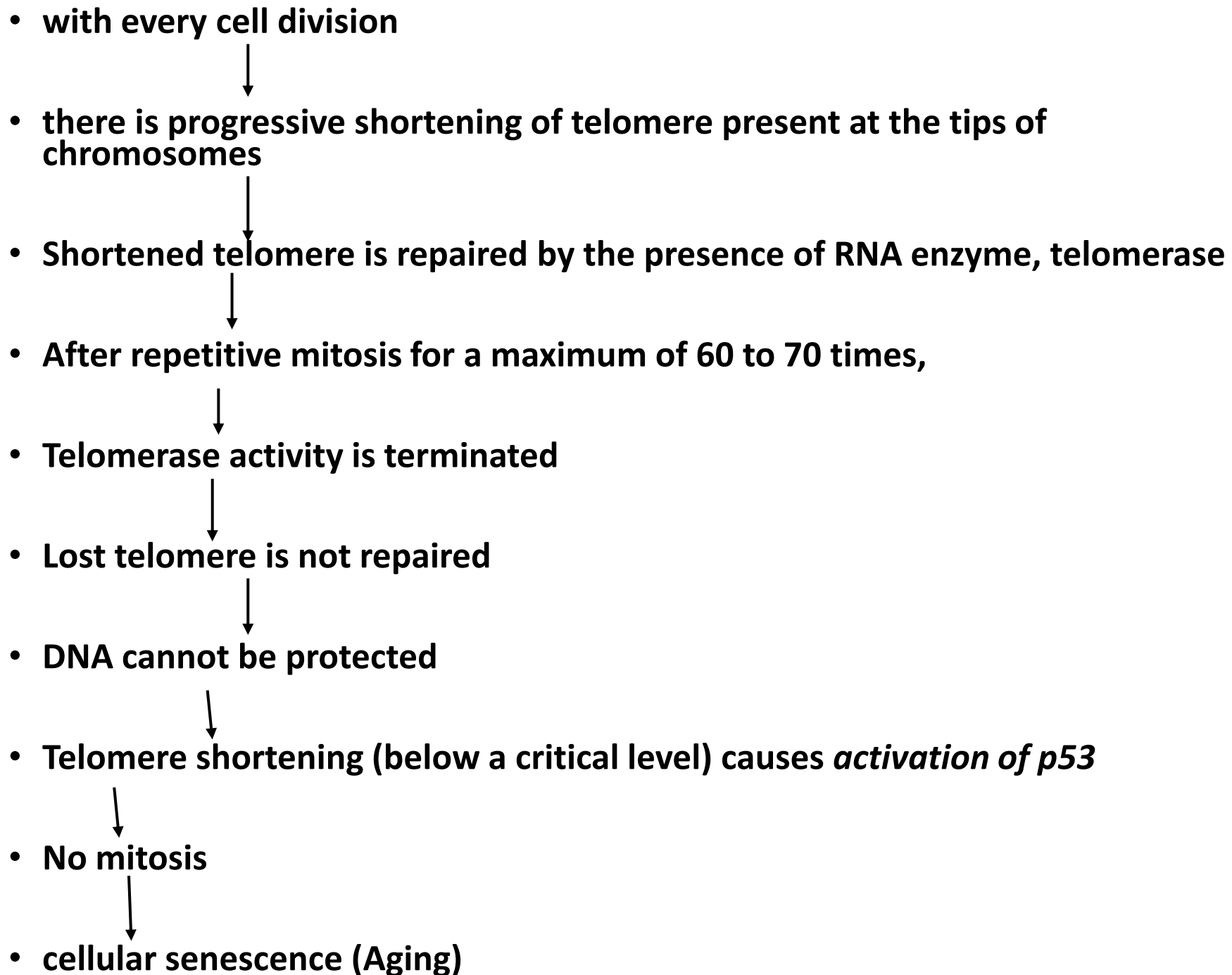


- **Telomeres** are short repeated sequences of DNA (TTAGGG) present at the linear ends of chromosomes that are important for protecting DNA
- With every cell division, there is progressive **shortening of telomere** present at the tips of chromosomes
- Telomere length is normally maintained by an enzyme called **telomerase**.
- Telomerase is a specialized RNA-protein complex that uses its own RNA as a template for adding nucleotides to the ends of chromosomes

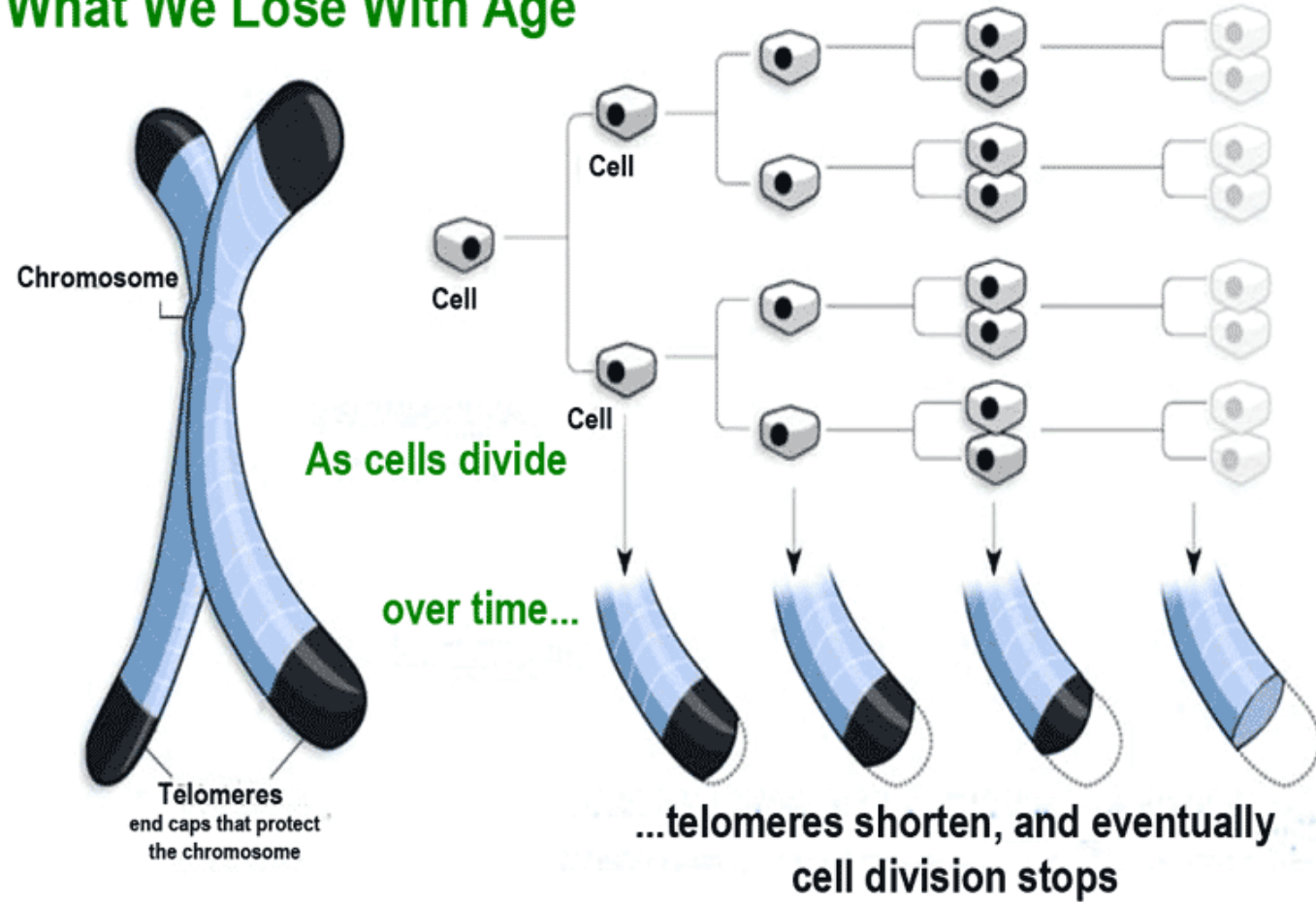


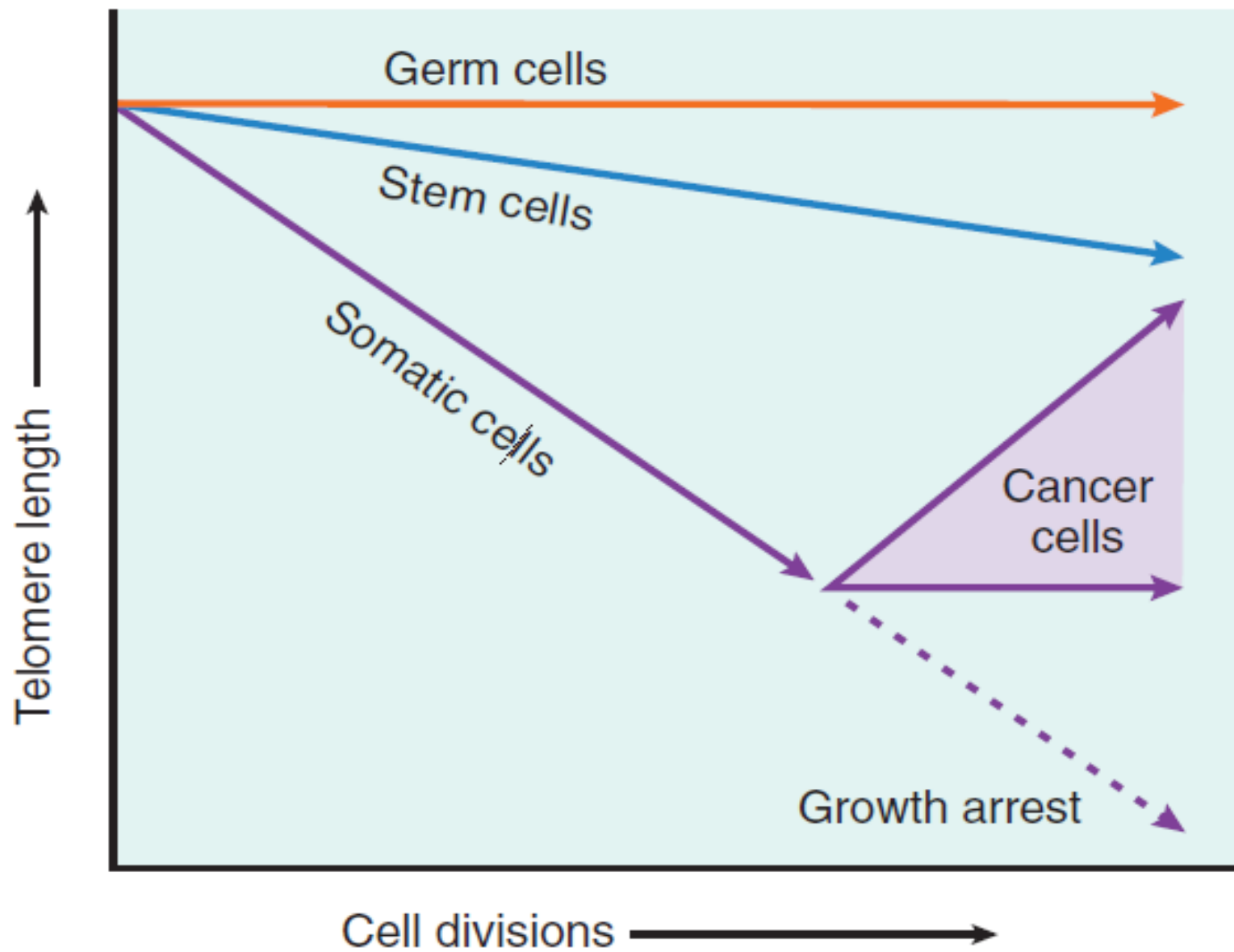
A

- **The activity of telomerase is decreased with age**
- Telomerase activity is highest in germ cells and present at lower levels in stem cells, very low in somatic tissues



## What We Lose With Age





## 2. Genetic control in invertebrates

- **Clock (clk)** genes responsible for controlling the rate and time of ageing identified in lower invertebrates
- e.g. clk-1 gene mutation in the metazoa, results in prolonging the lifespan

### 3. Diseases of accelerated ageing

- A heritable condition associated with signs of accelerated ageing process known as **progeria**
- **Werner's syndrome**, a rare autosomal recessive disease, characterised by premature ageing
- children is characterised by baldness, cataracts, and coronary artery disease.



## **4. Oxidative stress hypothesis (free radical-mediated injury)**

- With ageing, there is generation of toxic oxygen free radicals,  
↓
- which fail to get eliminated  
↓
- Their accumulation  
↓
- cell damage

## **5. Hormonal decline**

- With age, there is loss of secretion of some hormones resulting in their functional decline.

## **6. Defective host defenses**

- Ageing causes impaired immune function
- reduced ability to respond to microbes

## **7. Failure to renew**

- Ageing causes accumulation of senescent cells without corresponding renewal of lost cells.

# **PATHOGENESIS OF AGING**

- **1. TELOMERE THEORY**
- **2. Genetic control in invertebrates**
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- **7. Failure to renew**

A) Cellular changes :

- Decrease in cell size and number <sup>(AIIMS 01)</sup>
- Decreased in size and number of mitochondria <sup>(AI 97)</sup>
- Detachment of ribosomes from ER
- Increased number of phagolysosomal vacuoles
- Defective DNA repair
- Non-enzymatic glycosylation of protien <sup>(AI 97)</sup>

B) Connective tissue changes :

- There is loss of elasticity (wrinkling of skin)
- ↑ BP due to decreased elasticity of artery)
- Ground glass substance changes (cataract)
- Cartilage and bone changes (osteoarthritis, osteoporosis)

C) Decreased immunity :

- Decreased T cells, B cells, plasma cells and antibodies.

# ORGAN CHANGES IN AGEING

- 1. Cardiovascular system:** Atherosclerosis, arteriosclerosis with calcification, Mönckeberg's medial calcification, brown atrophy of the heart
- 2. Nervous system:** Atrophy of gyri and sulci, Alzheimer's disease, Parkinson's disease.
- 3. Musculoskeletal system:** Degenerative bone diseases, frequent fractures, muscular degeneration

**4. Eyes:** Deterioration of vision due to cataract and vascular changes in retina.

**5. Hearing:** Disability in hearing due to senility is related to otosclerosis.

**6. Immune system:** Reduced IgG response to antigens

**7. Skin:** Laxity of skin due to loss of elastic tissue.

**8. Cancers:** 80% of cancers occur in the age range of 50-80 years.

**QUESTIONS????**

**Dystrophic calcification means-**

*(PCI Dec. 97)*

- a) Calcification in destroyed tissue with normal calcium level in blood
- b)  $\uparrow$  level of  $\text{Ca}^{++}$  deposits
- c) Calcification in normal tissue seen in hyperparathyroidism
- d) Calcification in destroyed tissues with hypercalcemia



A

**Metastatic calcification is characterized by -**

- a) Hypercalcemia *(All India Dec.15 Pattern)*
- b) Hypocalcemia
- c) Eucalcemia
- d) None of the above

A

**Dystrophic calcification is seen in -**

- a) Milk alkali syndrome (CET Aug.13 Pattern)
- b) Atheromatous plaque
- c) Hyperparathyroidism
- d) Vitamin A intoxication

B

**Which of the following is not a common site for metastatic calcification -** *(AIIMS Nov 05)*

- a) Gastric mucosa
- b) Kidney
- c) Parathyroid
- d) Lung

C

**True about metastatic calcification -**

- a) Serum ca level is normal *(AIIMS May 09)*
- b) Occurs in dead/dying tissue
- c) Occurs in damaged heart valves
- d) Calcification starts in mitochondria



D

**Which of the following is associated with aging -**

- a) Reduced cross linkages in collagen
- b) Increased free radical injury *(AIIMS May 10)*
- c) Decreased Somatic mutations in DNA
- d) Increased superoxide dismutase levels

B

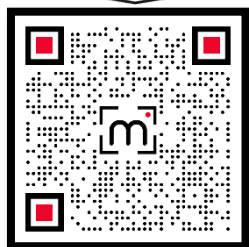
**All of the following statements are true for cell aging except -**

*(CET June14 Pattern)*

- a) Enlargement of telomere
- b) Decrease number of mitochondria
- c) Glycolysation of DNA
- d) Glycolysation of RNA

A

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# Thank you for being awake



*Scan or Click to watch  
Cell Adaptation & Injury*



*Scan or Click to watch  
Apoptosis & Necrosis*



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Inflammation*



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Haemodynamic Disorder*

